



Cognitive functioning as a predictor of response to comprehensive cognitive remediation



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ABSTRACT

Cognitive remediation is aimed at reducing cognitive impairments in severe mental illnesses such as schizophrenia, but little is known about whether severity of cognitive impairment predicts benefit from this intervention. To address this question, this study aggregated data from five randomized controlled trials (N = 300) of a standardized comprehensive, multimodal outpatient cognitive remediation program, the Thinking Skills for Work program, and evaluated whether baseline level of cognitive impairment differentially predicted improvement in cognitive functioning following cognitive remediation vs. usual services. Using standardized scores of neuropsychological functioning to designate “low average,” “moderate,” and “severe” levels of cognitive impairment, participants with greater cognitive impairment were found to benefit differentially more from cognitive remediation than usual services compared to less cognitively impaired participants. The findings were unaffected by statistically controlling for participant demographic and clinical characteristics. The findings suggest that individuals with the greatest cognitive impairment, for whom cognitive remediation was developed, are also most likely to benefit from this intervention.

1. Introduction

Impaired cognitive functioning is a common feature of severe mental illnesses such as schizophrenia, bipolar disorder, and treatment refractory major depression (Depp et al., 2012; Heinrichs, 2001; Porter et al., 2015). Lower cognitive functioning in areas such as attention, working memory, executive functions, and speed of processing is strongly associated with poorer psychosocial functioning, including quality of social relationships, role functioning, self-care skills, and independent living (Green, 2006; Green et al., 2015; Wykes, 1994). Furthermore, reduced cognitive abilities are a potent predictor of attenuated response to psychosocial treatments for severe mental illness, such as supported employment and social skills training (Kurtz, 2011).

In response to the abundant evidence about the importance of cognitive functioning to psychosocial adjustment in people with severe mental illness, cognitive remediation methods have been developed and evaluated. The most common of these methods include drill-and-practice of cognitive exercises, strategy coaching to improve performance on cognitive exercises, and teaching cognitive compensatory (or self-management) strategies to reduce the effects of impaired cognitive functioning in everyday life (McGurk et al., 2013). Over 50 randomized controlled trials of cognitive remediation for persons with severe mental illness have been conducted over the past several decades. Meta-

analyses show that cognitive remediation programs are effective at improving both cognitive and psychosocial functioning, with the impact on psychosocial functioning stronger in programs that provide both cognitive remediation and psychosocial treatment (compared to psychosocial treatment alone) than stand-alone cognitive remediation programs (McGurk et al., 2007; Revell et al., 2015; Wykes et al., 2011).

Despite the strong evidence supporting the effectiveness of cognitive remediation, limited research has examined which individuals are most likely to improve with treatment. Of particular relevance is whether an individual's baseline level of cognitive functioning is related to the extent to which they benefit from cognitive remediation. Greater cognitive impairment could make it more difficult to learn how to practice computer cognitive exercises, resulting in less practice, and contribute to greater frustration and reduced motivation to engage in cognitive remediation (Medalia and Richardson, 2005).

Several studies have explored whether initial levels of cognitive functioning predict cognitive improvement following cognitive remediation, with mixed results. Some studies have found that people with greater cognitive impairment benefit less from cognitive remediation (Lindenmayer et al., 2017; Wiedl et al., 2001), while others have reported the opposite, with lower cognitive functioning predicting greater benefit from cognitive remediation (Twamley et al., 2011). However, the majority of studies have found few cognitive predictors of

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benefit from treatment (Medalia and Richardson, 2005; Rodewald et al., 2014; Vita et al., 2013).

The lack of consistent findings across studies that evaluated cognitive functioning as a predictor of response to cognitive remediation is not surprising considering the methodological limitations of the research conducted thus far. Most of the studies have had modest sample sizes of under 60 participants receiving a particular type of cognitive remediation (Medalia and Richardson, 2005; Rodewald et al., 2014; Twamley et al., 2011; Vita et al., 2013; Wiedl et al., 2001), and two studies combined participants receiving different types of cognitive remediation (Lindenmayer et al., 2017; Vita et al., 2013). Three studies evaluated cognitive remediation interventions with as few as one (Wiedl et al., 2001) to ten sessions (Medalia and Richardson, 2005; Rodewald et al., 2014). Finally, none of the studies evaluated whether cognitive functioning predicted response to cognitive remediation compared to a control group. Determining the extent to which cognitive functioning differentially predicts benefit from cognitive remediation vs. usual treatment is crucial to making informed decisions as to which individuals can benefit and should be referred to this treatment.

The present analysis was conducted to overcome the methodological limitations of previous research on cognitive functioning as a predictor of response to cognitive remediation. To address this question, data from five randomized controlled trials evaluating a standardized comprehensive, multi-modal cognitive remediation intervention for persons with severe mental illness were combined and a meta-regression analysis was performed. The pooled sample size included more participants in the cognitive remediation program than in the largest of the prior studies (Lindenmayer et al., 2017), with approximately an equal number of control participants as well, and therefore had sufficient statistical power to address the research question.

2. Materials and methods

Data for the meta-regression were drawn from five randomized controlled trials of the Thinking Skills for Work program, a comprehensive, multi-modal cognitive remediation intervention that is integrated with vocational rehabilitation services (McGurk and Mueser, 2015; McGurk et al., 2005, 2009, 2015, 2016). All five of these studies were implemented in outpatient community mental health treatment settings with baseline and post treatment assessments of cognition and symptoms conducted by raters who were blind to treatment group. Improvement in neuropsychological test performance from baseline to post-treatment was the primary outcome of the analyses. All studies were approved by their respective IRB committees and all study participants provided written informed consent.

2.1. Participants

A total of 300 participants across the five studies were included in the analyses. All participants met the following inclusion criteria: a) 18 years of age or older; b) diagnosis of severe mental illness, which was defined as an Axis I diagnosis (with the exception of substance use disorder as the primary disorder) associated with severe functional impairments in work, social functioning, or self-care; c) not currently employed; d) a stated desire to work; and e) a history of an unsuccessful ending of a job that lasted less than three months (being fired from a job or quitting a job without another one in place), or recent failure to benefit from vocational rehabilitation services (not obtaining work for three months or more, or being fired from a job or quitting without another in place despite receiving services). Participant characteristics are presented for each study and the overall sample in Table 1.

The rates of participant attrition from research at the post-treatment assessment were 73%, 94%, 83%, 74%, and 94% for Study 1 through Study 5, respectively. Reasons for attrition included inability to contact participant, moved away from the treatment setting, psychiatric hospitalization, no longer interested in the study, and involvement in the

criminal justice system. “Exposure” to the Thinking Skills for Work program was defined as completion of a minimum of 6 (out of 24) computer cognitive training sessions. Rates of exposure to the program were 91%, 100%, 70%, 77%, and 93% for Study 1 through Study 5, respectively.

2.2. Study interventions

All five studies compared vocational rehabilitation alone to vocational rehabilitation enhanced with the Thinking Skills for Work program. Participants continued to receive the usual care available to them at their community treatment site, including pharmacological treatment, case management, vocational rehabilitation, and access to other psychosocial interventions. No restrictions were placed on the treatment services that study participants could receive during the study.

2.2.1. Thinking Skills for Work program

Only participants who were randomized to the Thinking Skills for Work program received cognitive remediation. This program is implemented by a trained clinician (a “cognitive specialist”) who provides the intervention and integrates it with the vocational rehabilitation services the participant is receiving. The program generally requires 6–9 months to implement, and is divided into five core components, including: 1) assessment of cognitive contributions to work attainment/performance difficulties; 2) 24 sessions of cognitive training using selected computerized cognitive exercises drawn from COGPACK software (Marker, 2014); 3) teaching cognitive self-management strategies to help participants “work around” persisting difficulties; 4) job search consultation with the participant and employment specialist to address problems obtaining jobs; and 5) job support consultation to address job performance difficulties or recent job losses.

2.2.2. Vocational rehabilitation programs

All participants were enrolled in the vocational rehabilitation program available at their center and continued to receive the same vocational services throughout the study, regardless of whether they were randomized to also receive the Thinking Skills for Work program. In Studies 1 and 4 (McGurk et al., 2005, 2015), the vocational rehabilitation program was supported employment (Becker and Drake, 2003); in Study 2 (McGurk et al., 2009) it was an internship-based vocational program; and in Studies 3 and 5 (McGurk and Mueser, 2015; McGurk et al., 2016) it was a diversified placement vocational program (Bond et al., 2007). In Study 3, participants in the Thinking Skills for Work program also received the Illness Management and Recovery program (Gingerich and Mueser, 2011). The details of each of the five study designs are summarized in Table 1.

2.3. Assessment

2.3.1. Premorbid intellectual functioning

Premorbid intellectual functioning was measured at baseline only with the Wide Range Achievement Test-III – Reading subtest (Wilkinson, 1993).

2.3.2. Cognitive functioning

A comprehensive battery of established neurocognitive tests was administered in all the studies to evaluate cognitive functioning across the broad range of domains, including attention, working memory, verbal learning and memory, speed of processing, and executive functioning. Studies 3 and 4 used the MATRICS Consensus Cognitive Battery (MCCB) (Nuechterlein et al., 2008). The other three studies were initiated before the MCCB was established, and employed a somewhat less extensive, but nevertheless comprehensive battery of measures, several of which overlapped with the MCCB. The cognitive tests for the two batteries were organized into the domains of cognitive functioning they tap, based on the organization of cognitive domains reported in the

Table 1
Study details, and demographic and diagnostic characteristics of participants by study (N = 300).

Study	Study 1 McGurk et al. (2005)	Study 2 McGurk et al. (2009)	Study 3 McGurk and Mueser, (2015)	Study 4 McGurk et al. (2015)	Study 5 McGurk et al. (2016)	
<i>Study Details</i>						
Location	Brooklyn	New York	Brooklyn	Manchester, NH/ Chicago	Brooklyn	
Study design	RCT ^a	RCT	RCT	RCT	RCT	
Experimental group	TSW ^b + SE ^c	TSW + VR-I ^d	TSW + VR-DP ^e	TSW + SE	TSW + IMR ^f + VR-DP	
Control group	SE Only	VR-I Only	VR-DP Only	SE Only	VR-DP Only	
<i>Participant Characteristics</i>						
N	44	34	61	107	54	Total 300
Age M (sd)	35.6 (12.4)	44.1 (9.1)	37.3 (10.7)	44.2 (11.1)	37.7 (9.4)	39.8 (10.5)
Hispanic N (%)	7 (15.9)	5 (14.7)	12 (19.7)	12 (11.2)	10 (18.5)	46 (15.3)
Race						
White N (%)	14 (31.8)	12 (35.3)	16 (26.2)	92 (86.0)	13 (24.1)	147 (49.0)
Black N (%)	29 (65.9)	21 (61.8)	43 (70.5)	11 (10.3)	33 (61.1)	137 (45.7)
Other N (%)	1 (2.3)	1 (2.9)	2 (3.3)	4 (3.7)	8 (14.8)	16 (5.3)
Never married N (%)	38 (86.4)	26 (76.5)	51 (83.6)	69 (64.5)	44 (81.5)	228 (76.0)
Completed high school N (%)	15 (34.1)	21 (61.8)	37 (60.7)	77 (72.0)	36 (66.7)	186 (62.0)
Schizophrenia spectrum N (%)	34 (77.3)	22 (64.7)	44 (72.1)	49 (45.8)	45 (83.3)	194 (64.7)
BPRS ^g M (sd)				2.1 (0.4)		
PANSS ^h M (sd)	2.4 (0.6)	2.2 (0.5)	1.9 (0.4)		2.3 (0.5)	2.1 (0.5)
WRAT ⁱ M (sd)	80.6 (18.7)	89.1 (13.6)	86.4 (15.5)	82.7 (10.2)	90.8 (16.3)	85.8 (14.9)
Cognitive composite M (sd)	27.6 (8.1)	29.5 (7.4)	30.7 (6.2)	24.0 (8.0)	30.5 (9.8)	28.5 (7.9)
Cognitive domains M (sd)						
Psychomotor Speed	27.7 (16.2)	29.9 (14.3)	34.0 (12.0)	27.1 (11.3)	35.7 (14.4)	30.8 (13.6)
Speed of Processing	26.0 (14.2)	34.8 (11.5)	35.2 (13.9)	27.1 (13.2)	34.2 (13.3)	31.5 (13.2)
Attention/Vigilance	39.1 (8.1)	38.4 (8.1)	38.2 (6.0)	31.8 (12.2)	33.2 (12.6)	36.1 (9.4)
Verbal Working Memory	38.4 (9.5)	41.2 (10.2)	41.4 (7.1)	29.5 (12.4)	37.5 (14.0)	37.6 (10.6)
Verbal Learning	24.7 (14.6)	36.2 (12.7)	35.1 (13.7)	32.8 (7.5)	36.8 (9.0)	33.1 (11.5)
Reasoning & Problem Solving	30.9 (4.1)	30.5 (7.6)	31.0 (7.7)	33.8 (8.1)	38.8 (9.1)	33.0 (7.3)
Cognitive Flexibility	-2.5 (14.8)	-6.1 (15.3)	-2.8 (13.6)	-16.0 (23.6)	-5.3 (22.5)	-6.5 (17.9)

^a RCT = randomized controlled trial.

^b TSW = Thinking Skills for Work program.

^c SE = Supported Employment program.

^d VR-I = Vocational Rehabilitation Internship program.

^e VR-DP = Vocational Rehabilitation Diversified Placement program.

^f IMR = Illness Management and Recovery program.

^g BPRS - Brief Psychiatric Rating Scale.

^h PANSS = Positive and Negative Syndrome Scale.

ⁱ WRAT = Wide Range Achievement Test—III, scaled scores.

McGurk et al. (2007) and Wykes et al. (2011) meta-analyses of cognitive remediation, which are summarized in Table 2.

Attention/vigilance. Digit Span Forward (Wechsler Adult Intelligence Scale- Revised) (Wechsler, 1981) (total correct); Continuous Performance Test- Identical Pairs (CPT-IP) (Cornblatt et al., 1988) (D prime).

Psychomotor speed. The Trail Making Test, Part A (Radford et al., 1978) was used in all 5 studies (seconds to complete).

Speed of processing. Digit Symbol Substitution Test, Wechsler Adult Intelligence Scale- Revised) (Wechsler, 1981) (total number correct); Symbol Coding Test, Brief Assessment of Cognition in Schizophrenia (Keefe et al., 2004) (total number correct).

Learning: California Verbal Learning Test (Delis et al., 1987) (total words recalled in learning trials 1–5); Hopkins Verbal Learning Test (Brandt, 1991) (total words recalled in learning trials 1–3).

Executive functioning: The Wisconsin Card Sorting Test (Berg, 1948) (total categories obtained); Neuropsychological Assessment Battery-Mazes (Stern and White, 2003) (total correct).

Cognitive flexibility. The Trail Making Test, Part B (Radford et al., 1978) was used in all five studies (completion time in seconds).

2.3.3. Psychiatric diagnosis and symptoms

Psychiatric diagnosis was ascertained by interviewers at baseline with the Structured Clinical Interview for DSM-IV (First et al., 1996).

Psychiatric symptoms were assessed with the Brief Psychiatric

Rating Scale-Expanded (Lukoff et al., 1986) in Study 4, and the Positive and Negative Syndrome Scale (Kay et al., 1987) in the other four studies. Both of these measures include behaviorally anchored ratings on seven-point scales, and share 16 items: anxiety, delusions/unusual thought content, suspiciousness/persecutory, hallucinations, somatic concern, depression, guilt feelings, grandiosity, disorientation, excitement, hostility, blunted affect, emotional withdrawal, tension, mannerisms and posturing, motor retardation, uncooperativeness, and conceptual disorganization. In order to develop a common index of overall psychopathology across all studies, the average rating across these items was computed.

2.4. Statistical analyses

Cognitive composite scores were formed for the primary data analyses. After reversing the scores on Trails A and B so that higher scores reflect better performance, all the individual measure raw scores were computed to *T*-scores for each of the tests included in the cognitive domains listed in Table 2. Then, the composite cognitive measure was created by computing the mean *T*-score across the seven cognitive domains.

To evaluate whether participants with lower levels of cognitive functioning at baseline differed in their benefit from the Thinking Skills for Work program compared to those with higher baseline cognitive

Table 2
Cognitive tests by cognitive domain.

Cognitive domain	Study 1 McGurk et al. (2005)	Study 2 McGurk et al. (2009)	Study 3 McGurk and Mueser, (2015)	Study 4 McGurk et al. (2015)	Study 5 McGurk et al. (2016)
Psychomotor speed					
Trail Making-A	X	X	X	X	X
Speed of processing					
Wechsler Adult Intelligence Scale-Revised-Digit Symbol	X	X			
Brief Assessment of Cognition in Schizophrenia-Symbol Coding			X	X	X
Attention/vigilance					
Wechsler Adult Intelligence Scale-Revised-Digit Span Forwards	X	X			
Continuous Performance Test-Identical Pairs			X	X	X
Verbal working memory					
Wechsler Adult Intelligence Scale-Revised-Digit Span Backwards	X	X			
Letter Number Span			X	X	X
Verbal learning					
California Verbal Learning Test	X	X			
Hopkin's Verbal Learning Test-Revised			X	X	X
Reasoning and problem solving					
Wisconsin Card Sorting	X	X			
Neuropsychological Assessment Battery- Mazes			X	X	X
Cognitive flexibility					
Trail Making-B	X	X	X	X	X

functioning, we used three different cut-off scores for the cognitive composite index to dichotomize the sample into low vs. high groups. The three cognition cut-off scores were chosen to reflect three levels of impairment: low average impairment or worse (T -score ≤ 40), moderate impairment or worse (T -score ≤ 23), and severe impairment (T -score ≤ 19) (Wechsler, 1981). Chi-square and t -test analyses were used to examine demographic and clinical differences within the low and high cognition groups for each of the three cut-offs. Change scores in cognitive functioning over the treatment period were then computed by subtracting the baseline cognitive composite score from the post-treatment composite cognitive score.

Three multiple regressions were conducted to examine whether cognitive functioning at baseline (low vs. high using each of the three cut-off scores), treatment group, or the treatment group by cognitive functioning interaction predicted improvement in cognitive functioning at post-treatment. Site was also included as a covariate in these analyses, with the largest site set as the reference site (McGurk et al., 2015). For these analyses, a main effect for baseline cognitive functioning group indicates that participants in either the high (or low) cognition group at baseline improved significantly more in cognitive functioning over the treatment period than those in the other group, and a main effect for treatment group indicates that participants in the Thinking Skills for Work program (or control condition) improved more over the treatment period than those in the other group. A significant baseline cognition group by treatment group interaction indicates that participants in one of the cognition groups (high or low) improved significantly more from cognitive remediation (the Thinking Skills for Work program) than participants in the other cognition group.

Sensitivity analyses were conducted to determine whether the findings were influenced by inclusion of psychiatric diagnosis, age, or symptom severity in the analyses. This was accomplished by including psychiatric diagnosis (schizophrenia or schizoaffective disorder vs. other) as a main effect and the diagnosis by treatment group interaction in the multiple regression analyses. Separate multiple regressions were conducted by including average psychiatric symptom severity and age as main effects and their interactions with treatment group.

3. Results

The low average cognition group (T -score ≤ 40) had a cognitive

score $M = 26.9$ ($N = 271$) and the high group had a cognitive score $M = 44.1$ ($N = 23$). The low moderate impairment group (T -score ≤ 23) had a cognitive score $M = 21.7$ ($N = 156$), and the high group had a cognitive score $M = 36.6$ ($N = 132$). The low severe cognitive impairment group (T -score ≤ 19) had a cognitive score $M = 14.5$ ($N = 42$) while the high group had a cognitive score $M = 31.2$ ($N = 248$).

Across each of the three baseline cognitive functioning cut-off scores used to divide the sample into low vs. high cognition groups, participants in the low cognition group were significantly more likely to have schizophrenia or schizoaffective disorder (vs. other diagnoses), have lower WRAT scores, and be of non-white race than those in the high cognition group. In addition, participants with above low average cognitive scores ($T > 40$) were significantly more likely to have completed high school than those with below low average scores; and participants with above moderate cognitive impairment ($T > 23$) were significantly more likely to be male than those with below moderate impairment.

The three multiple regression analyses predicting cognitive change included the following variables: site, treatment group, baseline cognition (T -score ≤ 40 for low average; T -score ≤ 23 for moderate impairment; T -score ≤ 19 for severe impairment), and the treatment group by baseline cognition interaction. All three overall regression models were statistically significant. In the regression examining the low average cognition cut-point ($T \leq 40$), neither the cognition group nor the cognition group by treatment group interaction effects were statistically significant, while the effects for site and treatment group were significant. In the two regressions with the lower cognition cut-points ($T \leq 23$ and $T \leq 19$), the effects for baseline cognition group, treatment group, the cognition by treatment interaction, and site were statistically significant (see Table 3). In all three models, participants in the lower baseline cognition group improved more following cognitive remediation than participants in the higher cognition group, whereas participants in both cognition groups who received usual treatment tended not to change over time in cognitive functioning (see Fig. 1a, 1b, and 1c).

The multiple regression analyses were repeated separately controlling for diagnosis, age, and baseline severity of psychiatric symptoms, but did not alter the main findings. Similarly, controlling for age and education in the multiple regressions had no effect on the results.

Table 3
Multiple regressions predicting cognitive change.

	β	t	p	df	F	R ²	p
Model 1- Low average cognition^a							
Treatment group	-.257	-4.217	< .001				
Cognition group	-.296	-1.652	.100				
Cognition × treatment interaction	.185	1.035	.302				
Site 1	.055	.819	.414				
Site 2	-.166	-2.551	.011				
Site 3	-.220	-3.368	.001				
Site 4	.070	1.052	.294				
Overall model				251	7.114	.169	< .001
Model 2- Moderate cognitive impairment^b							
Treatment group	-.383	-4.893	< .001				
Cognition group	-.617	-3.439	.001				
Cognition × treatment interaction	.499	2.696	.008				
Site 1	.084	1.279	.202				
Site 2	-.147	-2.230	.021				
Site 3	-.196	-3.064	.002				
Site 4	.072	1.086	.278				
Overall model				243	8.490	.201	< .001
Model 3- Severe cognitive impairment^c							
Treatment group	-.634	-4.254	< .001				
Cognition group	-.630	-3.358	.001				
Cognition × treatment interaction	.648	2.888	.004				
Site 1	.100	1.523	.129				
Site 2	-.141	-2.209	.028				
Site 3	-.198	-3.060	.002				
Site 4	.055	.841	.401				
Overall model				247	8.099	.191	< .001

Note: Site 5 was used as the reference for site comparisons.

^a Low average cognition includes T-scores ≤ 40.

^b Moderate cognitive impairment includes T-scores ≤ 23.

^c Severe cognitive impairment includes T-scores ≤ 19.

4. Discussion

The present study evaluated whether severity of cognitive impairment was related to cognitive improvement in persons with schizophrenia and other severe mental illnesses who were participants in five randomized controlled trials of a well standardized, comprehensive cognitive remediation program, the Thinking Skills for Work program. The findings indicated that participants in the cognitive remediation program improved more in neuropsychological test performance than those who received usual care, with those participants who had greater

levels of cognitive impairment benefitting significantly more than those with less severe impairment. Furthermore, the findings were replicated across two levels of cognitive impairment (moderate and severe impairment), and were unaffected by controlling for demographic or diagnostic characteristics, or severity of psychopathology.

In contrast to the analyses comparing participants with low vs. high cognitive functioning at baseline using the cut-points for moderate or severe impairment, the analysis using the cut-point for low average cognition or worse ($T \leq 40$) did not find a significant cognition group by treatment group interaction. Thus, while participants with moderate

Mean Change of Low Average Cognition Group vs. Average ($T > 40$)

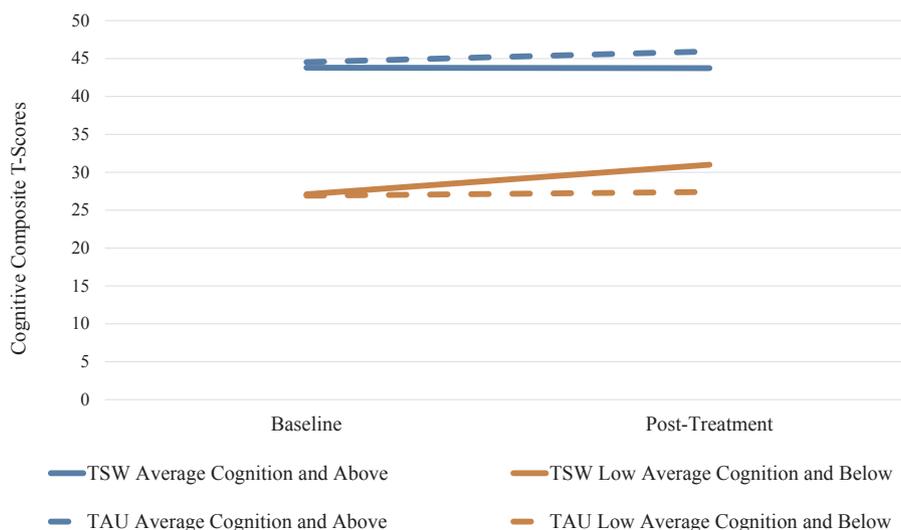


Fig. 1a. Mean Change of Low Average Cognition Group vs. Average ($T > 40$).

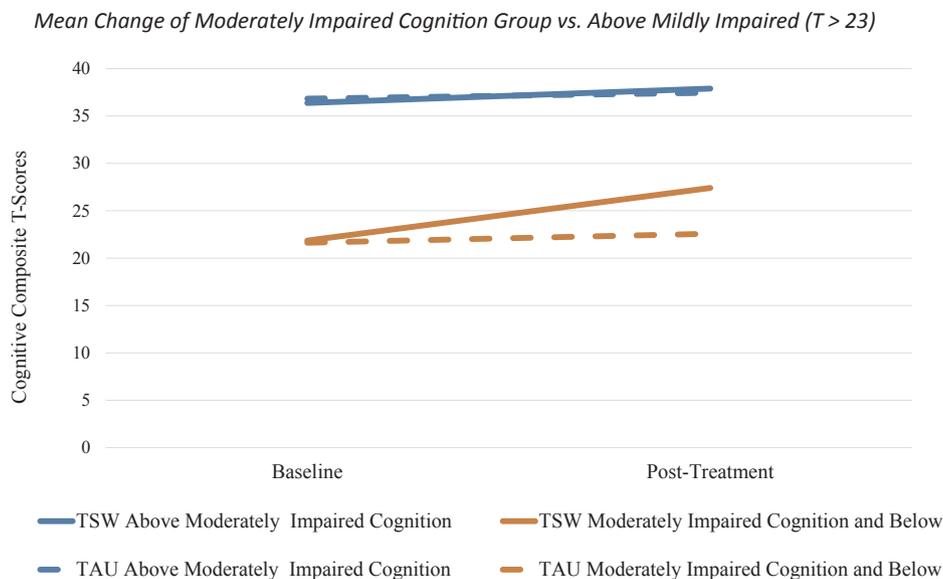


Fig. 1b. Mean Change of Moderately Impaired Cognition Group vs. Above Mildly Impaired ($T > 23$).

or severe levels of cognitive impairment at baseline who received cognitive remediation tended to improve more in cognitive functioning than less impaired participants, individuals whose cognitive functioning was relatively intact (i.e., above the low-average cut-off score) benefitted just as much from cognitive remediation as those with low average or worse cognitive functioning. It should be noted, however, that this analysis was statistically underpowered due to the relatively small number of participants whose baseline cognitive functioning was above the low-average cut-off score ($N = 23$).

Some prior research on cognitive predictors of response to cognitive remediation has produced null (Vita et al., 2013) or inconsistent results (Medalia and Richardson, 2005), although the findings of the present study are partially supported by the results of two small studies. In a sample of 23 participants who received 12 sessions of cognitive remediation based on teaching compensatory strategies, individuals with lower baseline cognitive functioning improved more at post-treatment than less impaired persons (Twamley et al., 2011). In a randomized controlled trial involving 77 participants assigned to either ten sessions of computer-based training in basic areas of cognitive functioning or

problem solving, Rodewald et al. (2014) reported that lower baseline planning ability predicted greater improvement in planning for participants who received problem solving training but not those who received basic cognitive training, whereas neither area of cognitive functioning at baseline predicted improvement in basic cognitive functioning for either group.

In comparison to the present findings, two other studies reported that lower levels of cognitive functioning predicted less improvement following cognitive remediation. Wiedl et al. (2001) reported that worse performance on the Degraded Stimulus Performance Test (Nuechterlein and Asarnow, 1986) predicted less learning on the Wisconsin Card Sorting Test (Berg, 1948) after a single session of special instructions and feedback on the test. However, it is unclear to what extent a single session of training cognitive performance on a neuropsychological test can be characterized as cognitive remediation, as most other programs provide multiple sessions of training across different cognitive areas.

In a study of 137 psychiatric inpatients who received approximately 36 sessions of cognitive remediation using Cogpack software based on

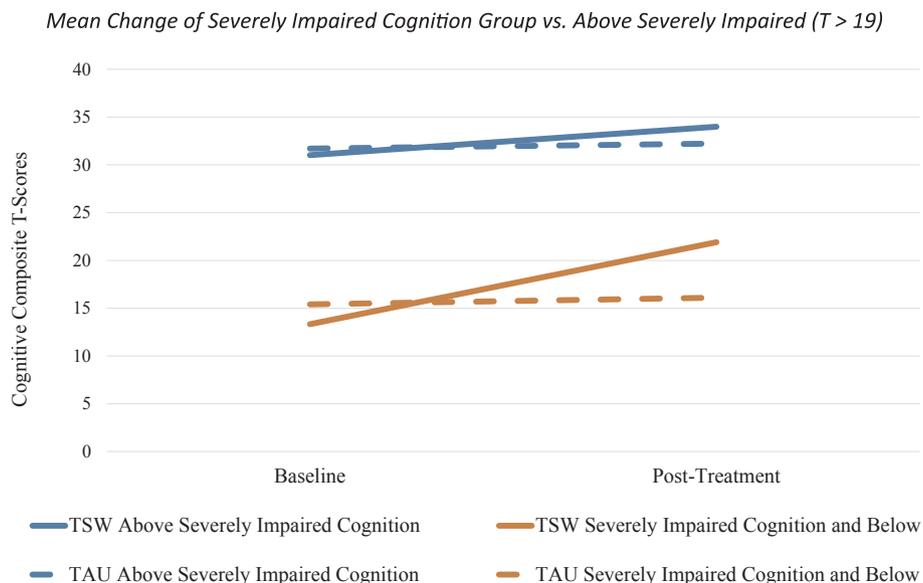


Fig. 1c. Mean Change of Severely Impaired Cognition Group vs. Above Severely Impaired ($T > 19$).

the Thinking Skills for Work program and “bridging groups” aimed at fostering generalization, Lindenmayer et al. (2017) found that participants with lower baseline cognitive functioning improved less on the MCCB than those with higher levels of initial neurocognitive functioning. Two related features of the Lindenmayer study may have implications for reconciling the opposite findings to those reported in the present study, despite similarities in the cognitive remediation programs used. First, the participants in Lindenmayer et al. were inpatients with significantly lower levels of baseline cognitive functioning than the outpatients included in the five studies reported here, as indicated by the lower overall *T*-scores between the samples ($T = 16.30$ vs. 28.58 , respectively). Second, cognitive training was conducted in 40 min groups of six to nine participants, with each person working at his or her own pace, and two (or more) staff members providing individual instruction or coaching as needed. In contrast, across the five studies reported here, cognitive training in the Thinking Skills for Work program was typically provided in 60–90 min sessions, either individually or in small groups of two or three participants. The combination of greater cognitive impairment and less intensive and individualized cognitive remediation in Lindenmayer et al. compared to these five studies included here suggests that participants with more severe cognitive impairment may require more intensive and personally tailored cognitive remediation to benefit as much or more than those less cognitively impaired. More work is needed to better understand how to provide cognitive remediation to address the more severe cognitive impairment often found in longer term psychiatric inpatients.

The present study has several methodological advantages over past research on this topic. First, prior research has explored cognitive predictors of response to cognitive remediation among participants who received the intervention, but has not evaluated the prediction of differential benefit from cognitive remediation compared to usual care, as in this study. The prediction of differential benefit from cognitive remediation provides more useful information than prediction within treatment recipients because it addresses the question of whether or not providing an intervention (cognitive remediation) is more likely to benefit some participants than others, a question with important clinical and resource implications.

Second, combining the data from five randomized controlled trials conducted in four different treatment settings and utilizing somewhat different neuropsychological batteries both permitted the formation of relatively large sample size for statistical analyses, and increased the generalizability of the results across participant characteristics and measures of cognitive functioning. Third, the cognitive remediation program studied (the Thinking Skills for Work program) was well standardized in a manual and employed selected cognitive exercises from an established cognitive training software package (Cogpack). In addition, high rates of participation in the Thinking Skills for Work program were present throughout all five studies, ensuring that participants had sufficient exposure to the cognitive remediation program. This high level of standardization of cognitive remediation increased the ability to obtain meaningful results by maximizing the replicability of the cognitive remediation methods across the studies.

The present findings suggest that those individuals with the greatest cognitive impairment stand to benefit the most from cognitive remediation in improving their cognitive functioning. These results confirm the most basic rationale for developing cognitive remediation methods in the first place—to reduce the cognitive impairment present in many individuals with schizophrenia and other severe mental illnesses (Spaulding et al., 1999; Wykes et al., 1999). The findings suggest that even outpatients with relatively severe cognitive impairment can benefit from a well-standardized, sufficiently intensive, facilitated cognitive remediation program.

Several limitations for the generalizability of these findings should be noted. First, although the symptom scales (Brief Psychiatric Rating Scale and Positive and Negative Syndrome Scale) overlap considerably, their anchors differ somewhat. These differences may have contributed

to the lack of significant effects of psychiatric symptoms. Second, because the long-term focus of the Thinking Skills for Work program is on improving employment outcomes (McGurk et al., 2005), participants in all five studies had competitive employment as a personal goal and were also enrolled in vocational rehabilitation programs. Thus, it is unknown whether the observed associations between baseline cognitive impairment and improvement in cognitive functioning during cognitive remediation would also be found if participants were receiving a different type of psychosocial rehabilitation, or no rehabilitation.

Third, the Thinking Skills for Work program is a comprehensive approach to cognitive remediation in which participants are engaged in a standardized curriculum of cognitive exercises drawn from Cogpack software, facilitated by a trained cognitive specialist who provides individualized coaching in the use of cognitive strategies during the exercises, and supplemented by teaching self-management strategies for improving day-to-day cognitive functioning. The incorporation of three major approaches to cognitive remediation into this program (i.e., cognitive exercises, strategy coaching on cognitive exercises, the teaching of cognitive self-management strategies) means that different associations could be found between cognitive impairment and response to intervention in cognitive remediation programs that include some but not all three of these cognitive remediation methods. Further research is needed to address these questions.

Conflicts of interest

None of the authors have any conflicts of interest to report.

Contributions

Drs. McGurk and Mueser designed the original five studies. DeTore and Ms. Byrd conducted the statistical analyses and Dr. DeTore, Dr. McGurk, and Dr. Mueser wrote the first draft of the manuscript. All authors contributed to and approved of the final manuscript.

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