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Cognitive Enhancement Therapy for Early Course Schizophrenia: Effects of a Two-Year Randomized Controlled Trial

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Abstract

Objective—The early application of cognitive rehabilitation may afford long-term functional benefits to patients with schizophrenia. This study examined the two-year effects of an integrated neurocognitive and social-cognitive rehabilitation program, cognitive enhancement therapy (CET), on cognitive and functional outcomes in early course schizophrenia.

Method—Early course outpatients (mean illness duration = 3.19±2.24 years) with schizophrenia or schizoaffective disorder were randomly assigned to CET ($n = 31$) or enriched supportive therapy (EST) ($n = 27$), an illness management intervention utilizing psychoeducation and applied coping strategies, and treated for 2 years. Multivariate composite indexes of cognitive, social adjustment, and symptomatology domains were derived from assessment batteries administered annually by computer-based tests and raters not blind to treatment assignment.

Results—Of the 58 patients randomized and treated, 49 and 46 completed 1 and 2 years of treatment, respectively. Intent to treat analyses showed significant differential effects favoring CET on social cognition, cognitive style, social adjustment, and symptomatology composites during the first year of treatment. After two years, moderate effects ($d = .46$) were observed favoring CET at enhancing neurocognitive function. Strong differential effects ($d > 1.00$) on social cognition, cognitive style, and social adjustment composites remained at year 2, and also extended to measures of symptomatology, particularly negative symptoms.

Conclusions—CET appears to be an effective approach to the remediation of cognitive deficits in early schizophrenia that may help reduce disability among this population. The remediation of such deficits should be an integral component of early intervention programs treating psychiatrically stable schizophrenia outpatients.

Schizophrenia is a chronic and disabling mental disorder that is characterized by related deficits in cognition, functioning, and adjustment. The significant personal and societal costs of the disorder (1), its frequent deteriorating course (2, 3), and the consistent negative prognosis associated with untreated illness (4), all highlight the importance of early applications of evidence-based interventions to reduce long-term morbidity (5). Cognitive impairments, in particular, are promising targets for early intervention due to their early emergence (6), persistence (7), and contribution to functional outcome (8). Unfortunately,

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few successful efforts have been directed toward the early treatment of cognitive deficits in schizophrenia.

Early course pharmacological studies of antipsychotic (e.g., olanzapine, perphenazine) and newer glutamatergic (e.g., glycine, D-cycloserine) agents have yielded only modest improvements in limited social and non-social cognitive domains that might, in part reflect repeated testing (9, 10, 11, 12). In addition, while several effective cognitive rehabilitation approaches exist for schizophrenia (13), the efficacy of these approaches when applied in the early course of the disorder has not been thoroughly assessed. Currently, the only two published randomized controlled trials of cognitive rehabilitation in early course patients have yielded mixed results (14, 15, 16). Further, these trials have been conducted exclusively with early- or childhood-onset patients and have employed relatively short-term (3 month) interventions that focus primarily on the remediation of neurocognitive deficits in attention, memory, and executive function. Long-term trials of cognitive rehabilitation approaches for early course patients are noticeably absent, and most approaches place little to no emphasis on the remediation of social cognition, which may be key to improving functional outcome (17).

Cognitive enhancement therapy (CET; 18) is an evidence-based developmental cognitive rehabilitation approach for the remediation of social and non-social cognitive deficits in schizophrenia that has conferred significant benefits for chronically ill patients. In a two-year randomized-controlled trial with 121 outpatients with schizophrenia who had been ill for an average of 15.70 ± 9.30 years, patients receiving CET demonstrated large and highly significant improvements in neurocognitive and social-cognitive function, as well as social adjustment (19). Further, these robust effects remained one year after treatment ended (20). Recently, we found initial support for the efficacy of CET for producing large improvements in social cognition among a preliminary sample of 38 early course schizophrenia patients who had completed 1 year of a 2-year randomized trial (21). However, data on other areas of cognition and functional outcome were not yet available for analysis, leaving open questions regarding the effects of CET on broader areas of cognition and the long-term functional significance of these initial social-cognitive effects. We now report on the complete cognitive and behavioral results from all 58 individuals who entered and were treated in this two-year trial of CET for early schizophrenia. Based on our previous study of CET with chronic outpatients, it was hypothesized that individuals receiving CET would demonstrate significant differential improvements over the course of treatment in processing speed, neurocognitive and social-cognitive function, as well as social adjustment, compared to a state-of-the-art enriched supportive control condition.

Method

Participants

Participants consisted of 58 early course outpatients who met diagnostic criteria (Structured Clinical Interview for DSM-IV [22]) for schizophrenia ($n = 38$) or schizoaffective disorder ($n = 20$). The one-year social-cognitive effects of CET on a subset ($n = 38$) of these individuals have been reported on previously (21). Eligible participants included individuals stabilized on antipsychotic medication with a diagnosis of schizophrenia, schizoaffective, or schizophreniform disorder who had experienced their first psychotic symptoms (including duration of untreated illness) within the past 8 years, had an $IQ > 80$, were not abusing substances for at least 2 months prior to study enrollment, and exhibited significant social and cognitive disability on the Cognitive Style and Social Cognition Eligibility Interview (19).

Participants were young with an average age of 25.92 ± 6.31 years, over two-thirds ($n = 40$) were male, and most were Caucasian ($n = 40$). Although participants were eligible for this study if they had their first psychotic symptoms (including duration of untreated illness) within the past 8 years, most (78%) had been ill for fewer than 5 years and the duration since first psychotic symptoms of enrolled patients was on average (3.19 ± 2.24 years) much less than the maximal eligible illness duration. While many participants had some college education ($n = 39$), most were not employed at baseline ($n = 43$).

Measures

A comprehensive battery of cognitive and behavioral measures was used to assess the effects of CET on cognition, adjustment, and symptomatology (see Table 1). In order to avoid excessive univariate inference testing that could inflate experiment-wise error rates, internally consistent multivariate composite indexes of these domains were computed. Individual measures were selected for these composites based on previous literature identifying the important domains of cognitive impairment in schizophrenia (23), field standards for adjustment and symptom assessment (24, 25), as well as previous CET studies (19, 20). Measures showing poor reliability (interitem $r < .10$) were excluded. Four composite indexes covering cognitive function were computed to represent speed of processing, neurocognition, dysfunctional cognitive style, and social cognition. Neurocognitive and processing speed measures reflect the relevant domains of neurocognitive impairment identified by the NIMH-MATRICES committee (26). Social cognition and cognitive style measures included those developed for our previous trial of CET, which have shown adequate reliability (19); and the NIMH-MATRICES recommended Mayer-Salovey-Caruso Emotional Intelligence Test (27), which has demonstrated adequate psychometric properties for assessing social cognition in schizophrenia (28, 29). A single composite index was computed for social adjustment and symptomatology, respectively, from multiple measures with well-documented psychometrics. Employment data were collected using the Major Role Adjustment Inventory (30), a 22-item, clinician-rated interview covering role adjustment in the domains of employment, family and household life, and social relationships. Information collected on employment in this instrument consists of vocational status, type of occupation, and number of hours a week worked at the time of the interview. Composite indexes were scaled to a baseline mean of 50 ± 10 , with lower scores reflecting better cognitive and behavioral functioning. Social cognition, neurocognition, and processing speed composites served as primary outcome measures. Secondary outcomes included the cognitive style and social adjustment composites. Although symptomatology was assessed, differential treatment effects on symptoms were not expected.

Treatments

Medication—All participants were maintained on Food and Drug Administration approved antipsychotic medications for the treatment of schizophrenia and schizoaffective disorder by a study psychiatrist. Medication changes were allowed, although every effort was made to stabilize patients on a tolerable and efficacious antipsychotic regimen prior to the initiation of psychosocial treatment. All patients were seen by a clinical nurse specialist at least biweekly to monitor medication side-effects and efficacy. Most patients (> 98%) were maintained on second-generation antipsychotics throughout the study, and no significant differences emerged with regard to antipsychotic dose, type, or clinician estimated compliance between treatment groups (see Table S1).

Cognitive enhancement therapy—CET is a comprehensive, developmental approach to the remediation of social and non-social cognitive deficits in schizophrenia that seeks to facilitate the development of adult social-cognitive milestones (e.g., perspective-taking,

social context appraisal) by shifting thinking from reliance on effortful, serial processing to a “gistful” and spontaneous abstraction of social themes. The treatment consists of approximately 60 hours of computer-assisted neurocognitive training in attention, memory, and problem-solving; and 45 social-cognitive group sessions that employ *in vivo* learning experiences to foster the development of social wisdom and success in interpersonal interactions. A broad, theoretically-driven array of social-cognitive abilities are targeted in the social-cognitive groups, which range from abstracting the “gist” or main point in social interactions to perspective-taking, social context appraisal, and emotion management (23, 31). Patients participate actively in the social-cognitive groups by responding to unrehearsed social exchanges, presenting homework, participating in cognitive exercises that focus on experiential learning, providing feedback to peers, and chairing homework sessions. CET typically begins with approximately 3 months of weekly 1-hour neurocognitive training in attention, after which patients begin the weekly 1.5-hour social-cognitive groups. Neurocognitive training then proceeds concurrently with social-cognitive groups throughout the remaining course of treatment. A complete description of the treatment has been provided elsewhere (18).

Enriched supportive therapy—Enriched supportive therapy (EST) is an illness management and psychoeducation approach that draws upon components of the basic and intermediate phases of the demonstrably effective personal therapy (32). In this approach, patients are seen on an individual basis to learn and practice stress management techniques designed to forestall late post-discharge relapse and enhance adjustment. The EST treatment is divided into two phases. Phase I focuses on basic psychoeducation about schizophrenia, the role of stress in the disorder, and ways to avoid/minimize stress. Phase II involves a personalized approach to the identification and management of life stressors that pose particular challenges to adequate social and role functioning. Patients move through the two phases of EST at their own pace, although each phase is typically provided for a year. Phase I was designed to be provided on a weekly basis, and Phase II was provided on a biweekly basis. Although no attempt was made to match CET and EST approaches with regard to hours of treatment, EST served as the active control for this trial, in part, to control for the potential effects of illness management and education interventions on outcome (33, 34), which are provided in both CET and EST. All psychosocial interventions were administered by masters-level psychiatric nurse specialists (S.J.C., A.L.D., and S.S.H.), and clinical supervision was provided by the treatment developers (G.E.H. and D.P.G.)

Procedures

Participants were recruited from inpatient and outpatient services at Western Psychiatric Institute and Clinic, Pittsburgh and nearby community clinics. Upon recruitment, patients were screened for eligibility in consensus conferences utilizing videotaped interviews. Eligible participants were randomly assigned to either CET or EST by a project statistician using computer-generated random numbers, and then treated for two years and assessed annually on the aforementioned measures of cognition and behavior. One-year assessments were conducted to assess intermediate improvement. Neurocognitive and some social-cognitive assessments (i.e., MSCEIT) were completed via computer-based tests or administered by trained neuropsychologists, and the remaining assessments were completed by study clinicians who had been extensively trained in their use and were not blind to treatment assignment. Figure 1 provides a description of the participant flow throughout the study. There were no significant differences between treatment conditions with regard to demographics, attrition, or symptomatology at baseline. However, as expected, individuals assigned to CET received significantly more hours of clinician contact (see Table S1). This research was conducted between August, 2001 and September, 2007, and was approved

annually by the University of Pittsburgh Institutional Review Board. All patients provided written informed consent prior to participation.

Data Analysis

Intent to treat analyses were conducted with all 58 patients who were randomized and received any exposure, regardless of how limited, to their respective treatment conditions. Treatment effects were analyzed in a sequential fashion in order to avoid excessive inference testing that could not be realistically corrected using Type I error correction algorithms. This was accomplished by first examining the main effects of treatment assignment on multivariate composite indexes of cognition and behavior using linear mixed-effects models, adjusting for potentially confounding demographic (age, gender, illness duration, and IQ) and medication (dose) effects. Subsequently, univariate main effects within composites were examined using the same mixed-effects strategy, only for those domains that demonstrated significant multivariate effects. All mixed-effects analyses used random intercept and slope models, and employed an autoregressive error structure most suitable for longitudinal data (35). Skewed data were handled using non-linear or rank transformations, and neuropsychological and processing speed outliers were handled by winsorization (36).

Results

Main Effects on Composite Indexes of Cognition and Behavior

We began our analysis of the effects of CET and EST by first examining their differential effects on multivariate composite indexes of cognition and behavior. As can be seen in Table 2, during the first year of treatment individuals receiving CET displayed significant and medium to large differential improvements in dysfunctional cognitive style, social cognition, social adjustment, and symptomatology compared to those receiving EST. After 2 years of treatment, highly significant and large differential effects were observed favoring CET for improving composite indexes of social cognition, cognitive style, social adjustment, and symptomatology (see Figure 2). In addition, CET patients demonstrated significant and medium-sized differential improvement on the neurocognitive composite by the second year of treatment.

Main Effects on Univariate Components of Cognitive and Behavioral Composite Indexes

Having demonstrated significant and large effects favoring CET for improving cognition and behavior on multivariate composite indexes by the second year of treatment, we proceeded to investigate the nature of these effects by examining differential rates of improvement for the individual components of these composites. As can be seen in Table 3, differential improvement on the neurocognitive composite was reserved for select measures of verbal memory, executive functioning and planning, and neurological soft signs. Differential effects on the cognitive style composite were centered around improving problems with motivation and disorganization, whereas effects on the social cognition composite were more broad and ranged from significant improvements in social and emotional information processing to improved interpersonal effectiveness and foresightfulness. Importantly, these large social-cognitive effects were evident not only on clinician-rated measures of social cognition, but were also observed on the performance-based MSCEIT.

Improvements favoring CET on behavioral composites of social adjustment and symptomatology were also broad. Significant effects were observed favoring CET with regard to employment, social functioning, global adjustment, activities of daily living, and instrumental task performance (see Table 3). A closer inspection of effects on employment indicated that significantly more patients receiving CET (54%) were actively engaged in

paid, competitive employment (assessed through clinician interviews using the Major Role Adjustment Inventory [30]) at the end of 2 years of treatment, compared to those receiving EST (18%), $\chi^2 = 4.93$, $df = 1$, $p = .026$. With regard to the symptom composite, significant differential effects favoring CET were observed on multiple measures of negative symptoms, as well as measures of anxiety and depression.

Discussion

Cognitive remediation has emerged as an effective method for ameliorating the cognitive deficits associated with schizophrenia that undermine functional recovery (13). Short-term trials conducted with childhood/early-onset patients focusing on neurocognitive dysfunction have suggested the potential benefits of cognitive remediation at the earliest stages of the illness (14, 15, 16). To our knowledge, this is the first study to examine the long-term effects of a comprehensive neurocognitive and social-cognitive rehabilitation program on broad domains of cognition and functioning when applied in early schizophrenia. Results from this two-year trial broadly support our hypotheses that CET would improve cognitive and behavioral outcomes among this population. Individuals receiving CET demonstrated substantial cognitive gains during the two years of treatment, particularly in social cognition, where a broad array of social-cognitive improvements were found on multiple performance-based and clinician-rated measures. Most importantly, while specific mediator analyses are needed and will be the focus of subsequent reports, these cognitive gains appear to have translated into significant reductions in disability. Individuals in CET exhibited marked improvements in employment, social functioning, and global adjustment, as well as reductions in negative symptoms compared to their EST counterparts. These effects, which could not be accounted for by group differences in antipsychotic medication use or differential rates of attrition, highlight the potential functional benefits of sufficient exposure to early cognitive rehabilitation in schizophrenia.

It is important to note that the largest cognitive effects observed during CET were in social cognition, a domain that has been linked to functional outcome (37) and remained largely unresponsive to pharmacological treatment (38). While neurocognitive effects were moderate in size, it was surprising that early course patients receiving CET did not show any significant improvement in processing speed, which is in contrast to our previous study with long-term patients (19). Comparison of average processing speed scores between this early course sample and those in our previous study indicated that early course patients performed significantly better on every measure of processing speed at baseline compared to chronic patients, all $t < -2.96$, all $df = 56$, all $p < .005$. In fact, the pre-treatment means of individuals receiving CET in this study were comparable to the processing speed of chronic patients after two years of CET treatment (19), pointing to the possibility of a ceiling effect for speed of processing. That processing speed and other aspects of attention are less impaired among early course patients is not novel (6, 39, 40), and this research suggests that more complex social-cognitive processes may be the most critical targets for early intervention programs. CET may serve as a key adjunct to pharmacotherapy in this regard.

Despite the efficacy of CET for improving cognition and behavior among early course patients, the results of this research need to be interpreted in the context of a number of limitations. The patients studied were mostly male and Caucasian, and the results of this investigation may not generalize to more diverse samples. Treatment groups were also not matched for the number of hours of clinician contact, therefore results could reflect the non-specific effects of increased clinician contact on outcome. In addition, assessing clinicians were not blind to the treatments to which patients were assigned. As such, rater bias cannot be ruled out as a possible explanation for treatment effects. However, effects on performance-based measures of social cognition were equally strong as clinician-rated

measures; and social adjustment effects were seen on an array of different measures, many of which leave little room for rater bias (e.g., employment - although employment data did rely largely on self-report). Further, robust neurocognitive effects were also found on performance-based measures of cognition, arguing against a substantial rater bias.

Increased familiarity with computerized testing associated with CET exposure may also explain some improvements in performance on computer-based neuropsychological tests. However, CET effects on neurocognition were seen primarily on paper and pencil examinations that bear little resemblance to computerized training software, suggesting that while it is possible CET influenced test-taking behavior in general, it is less likely that differential neurocognitive improvement favoring CET was the result of enhanced computer literacy or familiarity. In addition, within-composite analyses need to be interpreted with caution, as while a hierarchical approach was used to avoid excessively inflating Type I error, multiple univariate tests were conducted on within-composite measures. Finally, this research was characterized by a somewhat modest sample size ($n = 58$), which may have precluded the detection of smaller treatment effects. However, to our knowledge this is the largest and longest early course study of cognitive rehabilitation to date, and our results indicate that our *a priori* power analyses based on previous studies (19) guided us toward a sample size that was sufficient to reliably detect the medium to large CET effects observed in this study. Consequently, it would appear that a sufficient number of individuals were studied to provide an adequate evaluation of the efficacy of CET in early schizophrenia. A one-year post-treatment follow-up study is currently being completed to ascertain the durability of these effects and determine whether they are comparable to the sustained benefits achieved by chronic patients (20).

Conclusions

CET is recovery-phase treatment for the remediation of social and non-social cognitive deficits among stable outpatients with schizophrenia. The results of this investigation suggest the early application of CET may confer substantial benefits in cognitive functioning and broad domains of functional outcome among this population. Sufficient exposure to cognitive rehabilitation may be a vital, yet overlooked component to early intervention programs, ultimately providing the critical ingredients needed to help individuals recover from this disorder.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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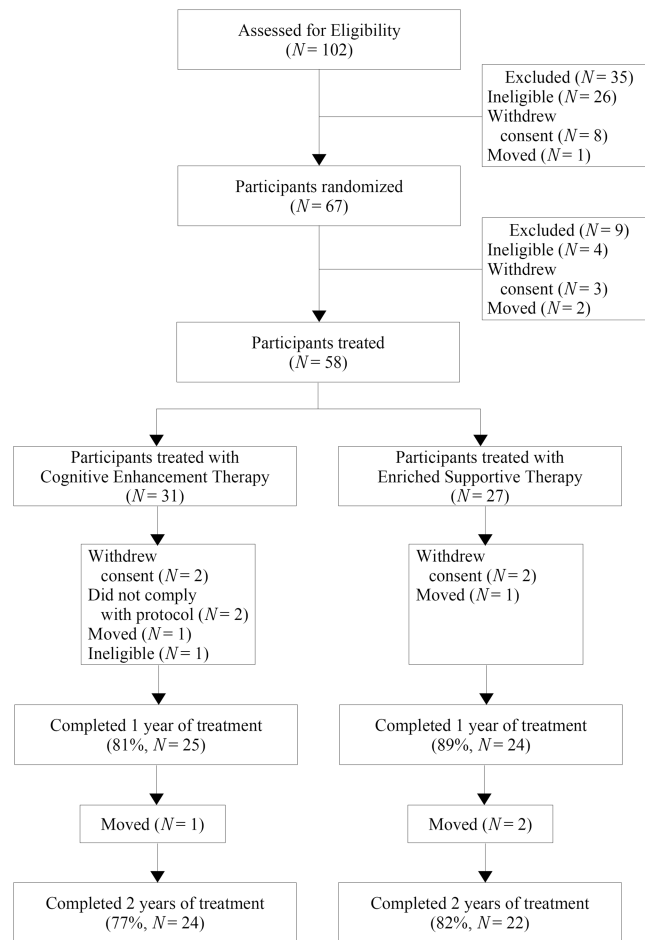


Figure 1. Participant Flow Over the Course of Two Years of a Randomized Trial of Cognitive Enhancement Therapy.

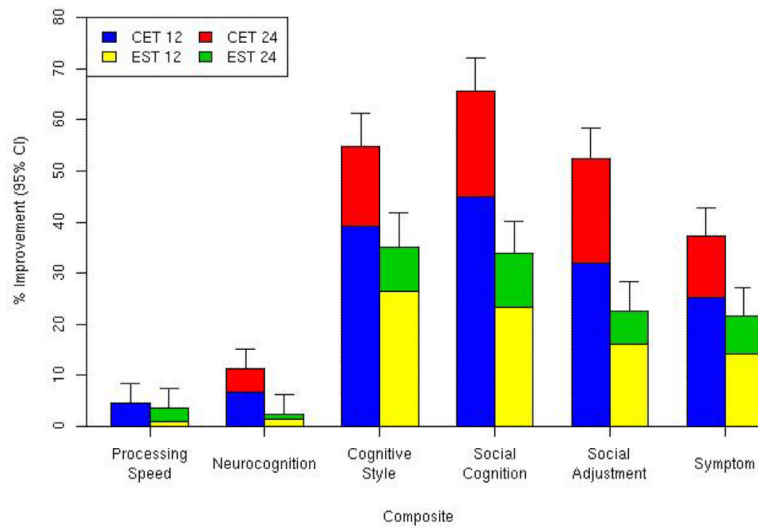


Figure 2. Differential Improvement of Persons Receiving Cognitive Enhancement Therapy Versus Enriched Supportive Therapy on Composite Indexes of Cognition and Behavior.

Table 1

Study Composite Indexes and Respective Component Measures of Cognition and Behavior.

Composite	Description	Component Measures
Processing Speed: $\alpha = .69$	Reaction time measures of speed of processing and attention	Simple reaction time (fixed and variable interstimulus interval) (41); Choice reaction time (dominant and non-dominant hand) (41); Visual-spatial scanning (42)
Neurocognition: $\alpha = .87$	Neuropsychological measures of verbal and working memory, executive functions, language ability, psychomotor speed, and neurological soft signs	Revised Wechsler Memory Scale (43); California Verbal Learning Test (44); Revised Wechsler Adult Intelligence Scale (45); Trails B (46); Wisconsin Card Sorting Test (47); Tower of London (48); Neurological Evaluation Scale (49)
Cognitive Style: $\alpha = .77$	Behavioral measures of impoverished, disorganized, and rigid dysfunctional cognitive styles	Cognitive Style and Social Cognition Eligibility Interview (19); Cognitive Styles Inventory (19)
Social Cognition: $\alpha = .70$	Performance-based measures of socio-emotional processing, and behavioral measures of foresightfulness, gistfulness, and other behavioral indicators of adequate social cognition	Mayer-Salovey-Caruso Emotional Intelligence Test (27); Social Cognition Profile (19); Cognitive Style and Social Cognition Eligibility Interview (19)
Social Adjustment: $\alpha = .87$	Behavioral measures of functional outcome in the domains of social and vocational functioning, and adjustment in major life roles	Social Adjustment Scale-II (25); Major Role Inventory (30); Global Assessment Scale (50); Performance Potential Inventory (19, 51)
Symptoms: $\alpha = .71$	Clinical and behavioral measures of positive and negative symptomatology, anxiety, depression, and self-esteem	Brief Psychiatric Rating Scale (24); Wing Negative Symptoms Scale (52); Raskin Depression Scale (53); Covi Anxiety Scale (54); Patient Subjective Response Questionnaire (55)

Table 2
Effects of Cognitive Enhancement Therapy and Enriched Supportive Therapy on Composite Indexes of Cognition and Behavior.

Composite	CET						EST						Between-Group Difference										
	Baseline		Year 1		Year 2		Baseline		Year 1		Year 2		Year 1		Year 2		Year 1		Year 2				
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	t ^a	d	p	t ^a	d	p	
Processing Speed	49.73	9.18	47.53	8.23	49.16	11.58	52.41	10.88	51.93	10.74	50.58	10.20	73	.470	.17	-.62	.540	-.13					
Neurocognition	50.39	9.47	47.01	8.81	44.67	7.55	47.15	10.63	46.52	9.64	46.04	9.93	1.73	.087	.27	2.32	.023	.46					
Cognitive Style	49.83	10.92	30.26	11.46	22.59	11.47	48.62	9.04	35.82	14.19	31.53	13.84	2.32	.023	.68	3.03	.003	1.02					
Social Cognition	48.76	11.61	27.34	10.50	17.87	13.50	48.63	7.95	37.97	11.89	33.28	11.66	4.15	<.001	1.08	4.98	<.001	1.55					
Social Adjustment	49.57	9.09	33.77	10.76	23.56	13.40	47.07	11.08	39.51	11.15	36.44	11.34	3.53	.001	.82	5.16	<.001	1.54					
Symptoms	48.93	10.32	36.56	10.33	30.75	10.68	48.33	9.82	41.45	11.46	37.84	8.46	2.07	.042	.55	2.74	.008	.77					

Note. Means are adjusted from linear mixed-effects models accounting for demographic effects and potential medication confounders. Composite scores are standardized with a baseline mean of 50±10, with lower scores indicating better cognitive or behavioral functioning.

CET = Cognitive enhancement therapy

EST = Enriched supportive therapy

^aDegrees of freedom for *t*-tests from mixed-effects models are *df* = 80 for processing speed, *df* = 81 for neurocognition, and *df* = 82 for cognitive style, social cognition, and symptom composites.

Table 3

Two-Year Univariate Effects of Cognitive Enhancement Therapy and Enriched Supportive Therapy on Cognition and Behavior.

Variable	CET						EST						Between-Group Difference		
	Baseline		Year 2		Year 2		Baseline		Year 2		Year 2		t	df	p
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD			
Neurocognition															
Verbal Memory															
WMS-R: Immediate recall ^a	21.68	7.25	22.52	5.85	23.41	7.23	23.76	8.57	23.76	8.57	23.76	8.57	-25	74	.806
WMS-R: Delayed recall ^a	15.92	8.13	18.32	6.46	18.85	8.24	21.18	8.83	21.18	8.83	21.18	8.83	-03	74	.974
CVLT: List A total recall ^b	50.56	12.95	52.42	9.37	54.44	11.97	50.60	12.56	50.60	12.56	50.60	12.56	-1.77	79	.080
CVLT: Short-term free recall ^c	9.86	3.21	11.34	2.37	10.77	3.65	10.29	4.07	10.29	4.07	10.29	4.07	-2.72	79	.008
CVLT: Long-term free recall ^c	10.20	3.41	10.83	2.76	11.50	3.60	10.99	3.46	10.99	3.46	10.99	3.46	-1.40	79	.166
Working Memory															
WAIS-R: Digit span ^d	10.20	2.19	10.25	2.00	9.68	2.28	10.13	2.34	9.68	2.28	10.13	2.34	.76	79	.447
Language															
WAIS-R: Vocabulary ^d	9.93	2.66	10.13	1.80	9.66	2.82	9.85	2.79	9.85	2.79	9.85	2.79	-03	79	.976
Executive Functions/Planning															
Trails B time, s ^e	63.71	21.31	49.60	10.92	61.25	24.59	59.06	24.47	61.25	24.59	59.06	24.47	2.08	79	.040
WAIS-R: Picture arrangement ^d	8.97	2.66	10.60	2.82	9.85	2.67	11.03	2.06	9.85	2.67	11.03	2.06	-64	79	.525
WCST: Categories achieved ^f	.74	.33	.81	.28	.77	.32	.75	.32	.77	.32	.75	.32	-86	80	.393
WCST: Perseverative errors ^g	11.35	8.14	10.08	7.04	9.62	6.25	8.80	6.32	9.62	6.25	8.80	6.32	.20	80	.842
WCST: Non-perseverative errors ^g	11.13	7.65	9.37	6.63	8.48	6.87	9.46	6.52	8.48	6.87	9.46	6.52	1.03	80	.306
WCST: % conceptual responses ^h	67.66	12.76	68.92	14.50	66.63	12.23	69.62	12.96	66.63	12.23	69.62	12.96	.37	79	.712
TOL: Ratio of initiation to execution time ⁱ	-2.04	.60	-1.37	.70	-1.77	.57	-1.56	.66	-1.77	.57	-1.56	.66	-2.10	80	.039
TOL: Move score ^j	41.64	19.34	38.47	21.84	39.04	16.58	39.23	25.80	39.04	16.58	39.23	25.80	.42	80	.674
Psychomotor Speed															

Variable	CET				EST				Between-Group Difference				
	Baseline		Year 2		Baseline		Year 2		M	SD	t	df	p
	M	SD	M	SD	M	SD	M	SD					
WAIS-R: Digit symbol ^d	8.88	2.47	10.14	3.08	8.43	2.60	9.71	2.97			.03	79	.976
Neurological Soft Signs													
NES: Cognitive-perceptual ^k	.51	.36	.16	.29	.40	.37	.37	.30			2.48	66	.016
NES: Repetition-motor ^k	.26	.36	.19	.33	.14	.28	.33	.37			2.35	66	.022
Cognitive Style													
Cognitive Style Eligibility Criteria													
Impoverished style ^l	10.72	2.79	6.12	2.22	10.80	2.58	7.87	2.58			2.51	79	.014
Disorganized style ^l	10.11	2.09	5.93	2.32	9.96	1.97	7.04	2.61			2.04	79	.044
Rigid style ^l	8.67	2.36	6.11	1.89	8.29	2.68	6.67	2.17			1.37	79	.173
Total impairment, disability, and social handicap ^m	29.50	5.01	18.18	4.64	29.11	4.34	21.59	5.98			2.57	79	.012
Highest cognitive style score ^l	11.88	1.75	7.41	1.94	11.79	1.48	8.85	2.06			2.85	79	.006
Cognitive Styles Inventory ⁿ													
Problems getting started	3.20	.82	1.84	.49	3.18	.71	2.50	.71			3.17	81	.002
Problems focusing	2.60	.66	1.83	.60	2.54	.70	2.07	.71			1.73	81	.088
Problems changing ideas	2.29	.56	1.85	.56	2.19	.65	2.00	.52			1.30	81	.196
Social Cognition													
Social Cognition Profile ^o													
Tolerant factor	3.30	.50	4.22	.54	3.12	.65	3.59	.57			-3.01	82	.004
Supportive factor	2.69	.56	4.01	.58	2.63	.45	3.31	.35			-4.54	82	<.001
Perceptive factor	2.42	.51	3.88	.62	2.37	.61	3.20	.56			-4.07	82	<.001
Confident factor	2.37	.54	3.74	.55	2.27	.50	3.05	.55			-3.53	82	.001
Social Cognition Eligibility Criteria ^o													
Interpersonal ineffectiveness	3.71	.73	2.22	.70	3.66	.76	3.01	.77			3.58	79	.001
Lack of foresight	3.59	.67	2.19	.79	3.63	.63	2.78	.61			2.09	79	.040

Variable	CET				EST				Between-Group Difference				
	Baseline		Year 2		Baseline		Year 2		M	SD	t	df	p
	M	SD	M	SD	M	SD	M	SD					
Gist extraction deficits	3.47	.93	1.98	.81	3.47	.94	2.46	.96	1.50	79	.137		
Adjustment to disability	3.04	.77	1.74	.66	2.97	.81	2.08	.64	1.42	79	.158		
MSCEIT ^p													
Perceiving emotions	91.51	15.99	95.86	17.25	97.77	16.46	92.90	15.96	-2.02	79	.047		
Facilitating emotions	90.38	18.50	94.09	17.56	99.63	16.28	99.22	15.73	-1.00	79	.321		
Understanding emotions	87.76	11.77	94.19	9.69	88.98	12.79	87.32	14.18	-2.30	79	.024		
Managing emotions	88.40	13.17	97.01	10.93	87.63	10.98	88.71	12.80	-2.74	79	.008		
Social Adjustment													
Employment													
MRAI: Employment ^q	2.96	1.30	1.81	1.14	2.86	1.36	2.60	1.20	2.18	80	.032		
PPI: Global work readiness ^r	1.52	.73	3.33	1.27	1.82	1.00	2.63	1.33	-2.87	81	.005		
SAS-II: Work affinity ^s	1.17	.72	.31	.65	1.04	.93	.99	.72	1.67	27	.106		
Social Functioning													
MRAI: Relationships outside the home ^t	2.68	.89	1.48	.66	2.50	.89	2.28	1.04	3.19	82	.002		
PPI: Social functioning ^r	2.57	.53	3.93	.58	2.68	.56	3.30	.64	-4.52	81	<.001		
SAS-II: Interpersonal anguish ^s	1.07	.64	.62	.49	.85	.64	.79	.62	2.41	82	.018		
SAS-II: Sexual relations ^u	3.34	1.31	2.70	1.65	3.69	1.03	3.43	1.25	.98	80	.329		
SAS-II: Primary relations ^s	.98	.74	.49	.60	1.05	.78	.67	.49	.46	59	.646		
SAS-II: Social leisure ^s	1.51	.84	.66	.70	1.09	.47	1.14	.68	3.92	82	<.001		
Global Functioning													
MRAI: Major role adjustment ^v	6.04	.97	3.81	1.91	6.10	1.23	5.16	1.52	2.67	82	.009		
MRAI: Overall functioning ^t	4.82	.35	3.77	1.18	4.54	.75	4.30	.74	3.24	82	.002		
Global Assessment Scale ^w	51.56	8.11	69.18	8.20	53.81	7.55	61.39	9.62	-4.29	82	<.001		
Mental status (PPI) ^t	2.89	.43	4.12	.52	2.98	.51	3.69	.57	-3.73	81	<.001		

Variable	CET				EST				Between-Group Difference		
	Baseline		Year 2		Baseline		Year 2		t	df	p
	M	SD	M	SD	M	SD	M	SD			
Activities of Daily living (PPI) ^f	2.62	1.16	4.25	.86	2.56	1.21	3.33	1.13	-3.40	81	.001
Instrumental task performance (PPI) ^f	2.30	.59	3.93	.73	2.45	.75	3.32	.80	-3.99	81	<.001
Self care (SAS-II) ^g	1.05	.65	.58	.43	1.14	.78	.95	.73	1.42	82	.159
Symptomatology											
Anxiety/Depression											
BPRS Anxiety-depression ^x	2.61	.85	1.97	.82	2.41	.68	2.28	.64	2.24	82	.028
Raskin depression ^y	6.63	2.77	3.85	1.24	6.21	1.98	4.70	1.49	1.96	82	.054
Covi anxiety ^y	5.72	2.08	4.79	1.43	5.89	2.22	5.35	1.53	.53	82	.595
Negative Symptoms											
BPRS Withdrawal-retardation ^x	2.74	1.20	1.63	.60	2.94	1.06	2.30	.78	1.99	82	.050
Wing negative symptoms ^z	18.30	4.14	11.01	3.44	18.25	3.63	13.99	3.79	2.47	82	.016
Thought Disorder (BPRS) ^x	2.12	1.14	1.71	.83	2.12	1.07	1.74	.80	.16	82	.872
Hostility (BPRS) ^x	1.61	.62	1.47	.51	1.75	.94	1.51	.62	-.64	82	.527
Global Degree of Illness ^x	4.22	.69	2.61	.87	4.27	.75	3.22	.90	2.42	80	.018
Self-Esteem ^{aa}	3.08	.80	3.90	.76	3.35	.71	3.74	.65	-1.97	74	.053

Note. Means are adjusted from linear mixed-effects models accounting for demographic effects and potential medication confounders.

BPRS = Brief Psychiatric Rating Scale, CET = Cognitive enhancement therapy, CVLT = California Verbal Learning Test, EST = Enriched supportive therapy, MRAI = Major Role Adjustment Inventory, MSCFIT = Mayer-Salovey-Caruso Emotional Intelligence Test, NES = Neurological Evaluation Scale, PPI = Performance Potential Inventory, SAS-II = Social Adjustment Scale-II, TOL = Tower of London, WAIS-R = Revised Wechsler Adult Intelligence Scale, WCST = Wisconsin Card Sorting Test, WMS-R = Revised Wechsler Memory Scale

^aPossible scores range from 0 to 50, with higher scores indicating better neurocognitive performance.

^bPossible scores range from 0 to 100, with higher scores indicating better neurocognitive performance.

^cPossible scores range from 0 to 20, with higher scores indicating better neurocognitive performance.

^dPossible scores range from 1 to 19, with higher scores indicating better neurocognitive performance.

^eScores are given in seconds, with higher scores indicating worse neurocognitive performance.

^fWCST categories achieved was rank order transformed due to non-normal distributions. Possible scores range from 0 to 1, with higher scores indicating better neurocognitive performance.

^gPossible scores range from 0 to 28, with higher scores indicating worse neurocognitive performance.

^hPossible scores range from 0 to 100, with higher scores indicating better neurocognitive performance.

ⁱTOL ratio of initiation to execution time was log transformed due to skewness. Higher scores indicate better neurocognitive performance.

^jPossible scores range from 0 to 189, with higher scores indicating worse neurocognitive performance.

^kPossible scores range from 0 to 1, with higher scores indicating more neurological soft signs.

^lPossible scores range from 3 to 15, with higher scores indicating greater cognitive dysfunction.

^mPossible scores range from 9 to 45, with higher scores indicating greater impairment from cognitive dysfunction.

ⁿPossible scores range from 1 to 5, with higher scores indicating greater cognitive dysfunction.

^oPossible scores range from 1 to 5, with higher scores indicating worse social-cognitive functioning.

^pScores are scaled with a mean of 100±50, with higher scores indicating better social-cognitive functioning.

^qPossible scores range from 1 to 4, with higher scores indicating worse adjustment.

^rPossible scores range from 1 to 5, with higher scores indicating better adjustment.

^sPossible scores range from 0 to 4, with higher scores indicating worse adjustment.

^tPossible scores range from 1 to 5, with higher scores indicating worse adjustment.

^uPossible scores range from 0 to 5, with higher scores indicating worse adjustment.

^vPossible scores range from 1 to 7, with higher scores indicating worse adjustment.

^wPossible scores range from 0 to 100, with higher scores indicating better adjustment.

^xPossible scores range from 1 to 7, with higher scores indicating greater symptomatology.

^yPossible scores range from 3 to 15, with higher scores indicating greater symptomatology.

^zPossible scores range from 6 to 30, with higher scores indicating greater symptomatology.

^{aa}Possible scores range from 1 to 5, with higher scores indicating greater self-esteem.