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

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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. _Methods:_ Early-course outpatients (mean±SD 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 two years. Multivariate composite indexes of cognitive, social adjustment, and symptom domains were derived from assessment batteries administered annually by computer-based tests and raters not blind to treatment assignment. _Results:_ Of the 58 participants who were randomly assigned and treated, 49 and 46 completed one year and two 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 for 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 in this population. The remediation of such deficits should be an integral component of early intervention programs treating psychiatrically stable schizophrenia outpatients. (_Psychiatric Services_ 60:1468–1476, 2009)

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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 frequently deteriorating course (2,3), and the consistent negative prognosis associated with untreated illness (4) 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 because of their early emergence (6), persistence (7), and contribution to functional outcome (8). Unfortunately, few successful efforts have been directed toward the early treatment of cognitive deficits in schizophrenia.

Pharmacological studies of antipsychotic agents (such as olanzapine and perphenazine) and newer glutamatergic agents (such as glycine and D-cycloserine) for early schizophrenia have yielded limited improvements in social and nonsocial cognitive domains that might in part reflect repeated testing (9,10). In addition, although several effective cognitive rehabilitation approaches exist for schizophrenia (11), the efficacy of these approaches when applied in the early course of the disorder has not been thoroughly assessed. The only two published randomized controlled trials of cognitive rehabilitation among patients with early-course schizophre-

nia have yielded mixed results (12–14). Further, these trials were conducted exclusively with patients with early- or childhood-onset illness and used relatively short-term (three-month) interventions that focused primarily on the remediation of neurocognitive deficits in attention, memory, and executive function. Long-term trials of cognitive rehabilitation approaches for patients with early-course schizophrenia 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 (15).

Cognitive enhancement therapy (CET) (16) is an evidence-based developmental cognitive rehabilitation approach for the remediation of social and nonsocial cognitive deficits in schizophrenia that has conferred significant benefits for patients with chronic illness. In a two-year randomized controlled trial with 121 outpatients with schizophrenia who had been ill for a mean±SD of 15.70±9.30 years, those receiving CET demonstrated large and highly significant improvements in neurocognitive and social-cognitive function, as well as social adjustment (17). Further, these robust effects remained one year after treatment ended (18).

Recently, we found initial support for the efficacy of CET in improving social cognition in a preliminary sample of 38 patients with early-course schizophrenia who had completed one year of a two-year randomized trial (19). However, data for 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 outpatients with long-term schizophrenia, we hypothesized that individuals receiving CET would demonstrate significant improvements over the course of treatment in processing speed, neurocognitive and social-cognitive function,

as well as social adjustment, compared with a state-of-the-art enriched supportive control condition.

Methods
Participants
Participants consisted of 58 outpatients who met diagnostic criteria of the Structured Clinical Interview for DSM-IV (20) for schizophrenia (N= 38) or schizoaffective disorder (N= 20). All were in the early course of their illness. The one-year social-cognitive effects of CET on a subset (N= 38) of these individuals have been reported previously (19). Eligible participants included those with schizophrenia, schizoaffective, or schizophreniform disorder whose illness had been stabilized on antipsychotic medication, who had experienced their first psychotic symptoms (including duration of untreated illness) within the past eight years, had an IQ ≥80, had not been abusing substances for at least two months before study enrollment, and showed significant social and cognitive disability on the Cognitive Style and Social Cognition Eligibility Interview (17).

Participants were young, with an average age of 25.92±6.31 years; over two-thirds (N=40, 69%) were male, and most were Caucasian (N=40, 69%), with 11 (19%) African American, six (10%) Asian, and one (2%) of other race-ethnicity. Although participants were eligible for this study if they had had their first psychotic symptom (including duration of untreated illness) within the previous eight years, most (N=45, 78%) had been ill for fewer than five years, with an average duration since first psychotic symptom of 3.19±2.24 years, much less than the maximal duration of illness for study eligibility. Although many had some college education (N=39, 67%), most were not employed at baseline (N=43, 74%).

Measures
A comprehensive battery of cognitive and behavioral measures was used to assess the effects of CET on cognition, adjustment, and symptomatology (Table 1) (21–38). To avoid excessive univariate inference testing that could inflate experimentwise error rates, we computed internally consistent multi-

variate composite indices of these domains. Individual measures were selected for these composites on the basis of literature that identifies the key domains of cognitive impairment in schizophrenia (39) and field standards for adjustment and symptom assessment (30,34), as well as previous CET studies (17,18). Measures with poor reliability (interitem r≤.10) were excluded. Four composite indices covering cognitive function were computed to represent speed of processing, neurocognition, dysfunctional cognitive style, and social cognition. Measures of neurocognitive ability and processing speed reflect the relevant domains of neurocognitive impairment identified by the NIMH-MATRICS Committee (National Institute of Mental Health–Measurement and Treatment Research to Improve Cognition in Schizophrenia) (40). Social cognition and cognitive style measures included those developed for our previous trial of CET, which have shown adequate reliability (17), and the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) (29) recommended by NIMH-MATRICS, which has demonstrated adequate psychometric properties for assessing social cognition in schizophrenia (41,42). A composite index was computed for social adjustment and symptomatology from multiple measures with well-documented psychometrics.

Employment data were collected with the Major Role Adjustment Inventory (31), 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 with 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.

Table 1

Composite indexes and component measures of cognition and behavior for assessing persons with early-course schizophrenia

Composite	Cronbach's α	Description	Component measures (reference)
Processing speed	.69	Reaction time measures of speed of processing and attention	Simple reaction time (fixed and variable interstimulus interval) (Ben-Yishay et al. [21]); choice reaction time (dominant and non-dominant hand) (21); visual-spatial scanning (Bracy [22])
Neurocognition	.87	Neuropsychological measures of verbal and working memory, executive functions, language ability, psychomotor speed, and neurological soft signs	Revised Wechsler Memory Scale (Wechsler [23]); California Verbal Learning Test (Delis et al. [24]); Wechsler Adult Intelligence Scale–Revised (Wechsler [25]); Trails B (Reitan & Walston [26]); Wisconsin Card Sorting Test (Heaton et al. [27]); Tower of London[a]; Neurological Evaluation Scale (Buchanan & Heinrichs [28])
Cognitive style	.77	Behavioral measures of impoverished, disorganized, and rigid dysfunctional cognitive styles	Cognitive Style and Social Cognition Eligibility Interview and the Cognitive Styles Inventory (Hogarty et al. [17])
Social cognition	.70	Performance-based measures of socioemotional processing, and behavioral measures of foresightfulness, "gistfulness," and other behavioral indicators of adequate social cognition	Mayer-Salovey-Caruso Emotional Intelligence Test (Mayer et al. [29]); Social Cognition Profile (Hogarty et al. [17]); Cognitive Style and Social Cognition Eligibility Interview (Hogarty et al. [17])
Social adjustment	.86	Behavioral measures of functional outcome in the domains of social and vocational functioning, and adjustment in major life roles	Social Adjustment Scale-II (Schooler et al. [30]); Major Role Inventory (Hogarty et al. [31]); Global Assessment Scale (Endicott et al. [32]); Performance Potential Inventory (Hogarty et al. [17]; DHHS[b] [33])
Symptoms	.71	Clinical and behavioral measures of positive and negative symptomatology, anxiety, depression, and self-esteem	Brief Psychiatric Rating Scale (Overall & Gorham [34]); Wing Negative Symptoms Scale (Wing [35]); Raskin Depression Scale (Raskin et al. [36]); Covi Anxiety Scale (Lipman [37]); Patient Subjective Response Questionnaire (Hogarty et al. [38])

[a] Culbertson WC, Zillmer EA: Tower of London-DX manual. Unpublished manuscript, 1996

[b] Department of Health and Human Services

Treatments

Medication. All participants received Food and Drug Administration–approved antipsychotic medications for the treatment of schizophrenia, schizoaffective disorder, and schizophreniform disorder as indicated by a study psychiatrist. Medication changes were allowed, although every effort was made to stabilize participants on a tolerable and efficacious antipsychotic regimen before the initiation of psychosocial treatment. All participants were seen by a clinical nurse specialist at least biweekly to monitor medication side effects and efficacy. Most participants (>98%) were given second-generation antipsychotics throughout the study, and no significant differences emerged with regard to antipsychotic dosage, type, or clinician-estimated compliance between treatment groups. [A table detailing the between-group differences in baseline demographic, clinical, and medication characteristics is available as an online supplement to this article at ps.psychiatryonline.org.]

Cognitive enhancement therapy. CET is a comprehensive, developmental approach to the remediation of social and nonsocial cognitive deficits in schizophrenia. It seeks to facilitate the development of adult social-cognitive milestones (such as perspective taking and appraisal of one's social context) 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 use experiential learning opportunities 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 (39,43). Participants engage 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 three months of weekly one-hour neurocognitive training in attention, after which participants 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 (16).

Enriched supportive therapy. En-

riched supportive therapy (EST) is an illness management and psychoeducation approach that draws on components of the basic and intermediate phases of the demonstrably effective personal therapy (44). In this approach, outpatients are seen on an individual basis to learn and practice stress management techniques designed to forestall late postdischarge relapse and enhance adjustment. The EST treatment is divided into two phases. Phase 1 focuses on basic psychoeducation about schizophrenia, the role of stress in the disorder, and ways to avoid or minimize stress. Phase 2 involves a personalized approach to the identification and management of life stressors that pose particular challenges to adequate social and role functioning. Participants move through the two phases of EST at their own pace, although each phase is typically provided for a year. By design, phase 1 was provided on a weekly basis, and phase 2 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 on outcome of illness management and education interventions (45), which are provided in both CET and EST. All psychosocial interventions were administered by three master's-level psychiatric nurse specialists, and clinical supervision was provided by the two treatment developers.

Procedures
Outpatients were recruited between August 2001 and January 2006 from inpatient and outpatient services at Western Psychiatric Institute and Clinic in Pittsburgh and from nearby community clinics. After recruitment, patients were screened for eligibility in consensus conferences showing videotaped interviews. Eligible persons were randomly assigned to either CET or EST by a project statistician using computer-generated random numbers. Participants were 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. Neurocogni-

tive and some social-cognitive assessments (such as the 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. [A figure that depicts the participant flow throughout the study is available as an online supplement to this article at ps.psychiatryonline.org.] There were no significant differences between treatment conditions with regard to demographic characteristics, attrition from the study, or symptomatology at baseline. However, as expected, individuals assigned to CET received significantly more hours of clinician contact [see the supplemental table at ps.psychiatryonline.org].

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 before their participation began.

Data analysis
Intent-to-treat analyses were conducted with all 58 participants who were randomly assigned to either CET or EST 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 with type I error correction algorithms. We accomplished this by using linear mixed-effects models to first examine the main effects of treatment assignment on multivariate composite indexes of cognition and behavior while adjusting for potentially confounding demographic (age, gender, illness duration, and IQ) and medication (dose) effects. Univariate main effects within composites were then examined with the same mixed-effects strategy for only the domains that had significant multivariate effects. All mixed-effects analyses used random intercept and slope models and an autoregressive error structure most suitable for longitudinal data (46).

Skewed data were handled by using nonlinear or rank transformations, and neuropsychological and processing speed outliers were handled by winsorization (47).

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 effects on multivariate composite indexes of cognition and behavior. In the first year of treatment, persons receiving CET had significant and medium to large differential improvements in dysfunctional cognitive style, social cognition, social adjustment, and symptomatology compared with those receiving EST (Table 2). After two years of treatment, highly significant and large differential effects were observed favoring CET on the composite indexes of cognitive style, social cognition, social adjustment, and symptomatology (Figure 1). In addition, CET participants showed significant and medium-size improvement on the neurocognitive composite by the second year of treatment.

Univariate effects on cognitive and behavioral composite indexes
Having demonstrated significant and large effects of CET in 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. Improvement on the neurocognitive composite was seen in select measures of verbal memory, executive functioning and planning, and neurological soft signs (Table 3). Differential effects on the cognitive style composite centered on improvements with motivation problems and disorganization, whereas effects on the social cognition composite were broader and ranged from significant improvements in social and emotional information processing to improved interpersonal effectiveness and foresightfulness. These large social-cognitive effects were evident not only on clinician-rated measures of social cogni-

Table 2

Scores on composite indices of cognition and behavior for persons in the early course of schizophrenia who received cognitive enhancement therapy or enriched supportive therapy[a]

Composite	Cognitive enhancement therapy						Enriched supportive therapy						Between-group difference					
	Baseline		Year 1		Year 2		Baseline		Year 1		Year 2		Year 1			Year 2		
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	t^b	p	d	t^b	p	d
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	23.65	13.48	47.07	11.08	39.50	11.15	36.43	11.34	3.51	.001	.82	5.11	<.001	1.53
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

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

[b] Degrees of freedom for t tests from mixed-effects models are 80 for processing speed, 81 for neurocognition, and 82 for cognitive style, social cognition, social adjustment, and symptoms composites.

tion but also on the performance-based MSCEIT.

Improvements favoring CET on behavioral composites of social adjustment and symptomatology were also broad. Significant effects of CET were observed with regard to voca-

tional and social functioning, global adjustment, activities of daily living, and instrumental task performance (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 [31]) at the end of two years of treatment, compared with recipients of EST (18%) (χ^2=4.93, df=1, p=.026). With regard to the symptom composite, significant effects of CET were observed on multiple measures of negative symptoms, as well as on measures of anxiety and depression.

Figure 1

Improvement among persons in the early course of schizophrenia who received two years of CET or EST[a]
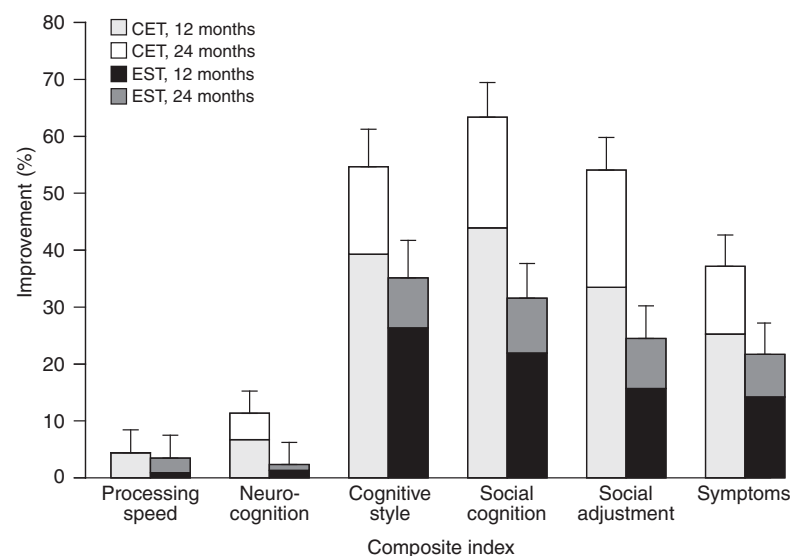
[a] CET, cognitive enhancement therapy; EST, enriched supportive therapy. Error bars indicate 95% confidence intervals.

Discussion

Cognitive rehabilitation has emerged as an effective method for ameliorating the cognitive deficits associated with schizophrenia that undermine functional recovery (11). Short-term trials conducted with patients who had childhood- or early-onset schizophrenia and that focused on neurocognitive dysfunction have suggested the potential benefits of cognitive rehabilitation at the earliest stages of the illness (12–14). 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 for this population.

Table 3

Univariate analysis of measures of cognition and behavior of persons in the early course of schizophrenia after two years of cognitive enhancement therapy or enriched supportive therapy

| | Cognitive enhancement therapy[a] | | | | Enriched supportive therapy[a] | | | | Between-group difference | | |
| | Baseline | | Year 2 | | Baseline | | Year 2 | | | | |
Variable[b]	M	SD	M	SD	M	SD	M	SD	t	df	p
Neurocognition											
Verbal memory											
WMS-R: immediate recall[c]	21.68	7.25	22.52	5.85	23.41	7.23	23.76	8.57	−.25	74	.806
WMS-R: delayed recall[c]	15.92	8.13	18.32	6.46	18.85	8.24	21.18	8.83	−.03	74	.974
CVLT: list A total recall[d]	50.56	12.95	52.42	9.37	54.44	11.97	50.60	12.56	−1.77	79	.080
CVLT: short-term free recall[e]	9.86	3.21	11.34	2.37	10.77	3.65	10.29	4.07	−2.72	79	.008
CVLT: long-term free recall[e]	10.2	3.41	10.83	2.76	11.50	3.60	10.99	3.46	−1.40	79	.166
Working memory											
WAIS-R: digit span[f]	10.2	2.19	10.25	2.00	9.68	2.28	10.13	2.34	.76	79	.447
Language: WAIS-R: vocabulary[f]	9.93	2.66	10.13	1.80	9.66	2.82	9.85	2.79	−.03	79	.976
Executive functions and planning											
Trails B time (seconds)[g]	63.71	21.31	49.60	10.92	61.25	24.59	59.06	24.47	2.08	79	.04
WAIS-R: picture arrangement[f]	8.97	2.66	10.60	2.82	9.85	2.67	11.03	2.06	−.64	79	.525
WCST: categories achieved[h]	.74	.33	.81	.28	.77	.32	.75	.32	−.86	80	.393
WCST: perseverative errors[i]	11.35	8.14	10.08	7.04	9.62	6.25	8.80	6.32	.20	80	.842
WCST: nonperseverative errors[i]	11.13	7.65	9.37	6.63	8.48	6.87	9.46	6.52	1.03	80	.306
WCST: conceptual responses (%)[d]	67.66	12.76	68.92	14.50	66.63	12.23	69.62	12.96	.37	79	.712
TOL: ratio of initiation to execution time[j]	−2.04	.60	−1.37	.70	−1.77	.57	−1.56	.66	−2.10	80	.039
TOL: move score[k]	41.64	19.34	38.47	21.84	39.04	16.58	39.23	25.80	.42	80	.674
Psychomotor speed: WAIS-R: digit symbol[f]	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[l]	.51	.36	.16	.29	.40	.37	.37	.30	2.48	66	.016
NES: repetition-motor[l]	.26	.36	.19	.33	.14	.28	.33	.37	2.35	66	.022
Cognitive style											
Cognitive style eligibility criteria											
Impoverished style[m]	10.72	2.79	6.12	2.22	10.80	2.58	7.87	2.58	2.51	79	.014
Disorganized style[m]	10.11	2.09	5.93	2.32	9.96	1.97	7.04	2.61	2.04	79	.044
Rigid style[m]	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[n]	29.50	5.01	18.18	4.64	29.11	4.34	21.59	5.98	2.57	79	.012
Highest cognitive style score[m]	11.88	1.75	7.41	1.94	11.79	1.48	8.85	2.06	2.85	79	.006
Cognitive Styles Inventory[o]											
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	.69	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	.04
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	1.92	1.21	2.87	1.36	2.85	1.20	1.87	80	.065
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

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Table 3

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Variable[b]	Cognitive enhancement therapy[a]				Enriched supportive therapy[a]				Between-group difference		
	Baseline		Year 2		Baseline		Year 2				
	M	SD	M	SD	M	SD	M	SD	t	df	p
Social functioning											
MRAI: relationships outside the home	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[t]	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[u]	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[v]	51.56	8.11	69.18	8.20	53.81	7.55	61.39	9.62	−4.29	82	<.001
PPI: mental status[r]	2.89	.43	4.12	.52	2.98	.51	3.69	.57	−3.73	81	<.001
PPI: activities of daily living[r]	2.62	1.16	4.25	.86	2.56	1.21	3.33	1.13	−3.40	81	.001
PPI: instrumental task performance[r]	2.30	.59	3.93	.73	2.45	.75	3.32	.80	−3.99	81	<.001
SAS-II: self-care[s]	1.05	.65	.58	.43	1.14	.78	.95	.73	1.42	82	.159
Symptomatology											
Anxiety and depression											
BPRS: anxiety-depression[w]	2.61	.85	1.97	.82	2.41	.68	2.28	.64	2.24	82	.028
Raskin depression[x]	6.63	2.77	3.85	1.24	6.21	1.98	4.70	1.49	1.96	82	.054
Covi anxiety[x]	5.72	2.08	4.79	1.43	5.89	2.22	5.35	1.53	.53	82	.595
Negative symptoms											
BPRS: withdrawal-retardation[w]	2.74	1.20	1.63	.60	2.94	1.06	2.3	.78	1.99	82	.050
Wing negative symptoms[y]	18.30	4.14	11.01	3.44	18.25	3.63	13.99	3.79	2.47	82	.016
BPRS: thought disorder[w]	2.12	1.14	1.71	.83	2.12	1.07	1.74	.80	.16	82	.872
BPRS: hostility[w]	1.61	.62	1.47	.51	1.75	.94	1.51	.62	−.64	82	.527
Global Degree of Illness[w]	4.22	.69	2.61	.87	4.27	.75	3.22	.90	2.42	80	.018
Self-esteem[r]	3.08	.80	3.90	.76	3.35	.71	3.74	.65	−1.97	74	.053

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

[b] WMS-R, Revised Wechsler Memory Scale; CVLT, California Verbal Learning Test; WAIS-R, Revised Wechsler Adult Intelligence Scale; WCST, Wisconsin Card Sorting Test; TOL, Tower of London; NES, Neurological Evaluation Scale; MSCEIT, Mayer-Salovey-Caruso Emotional Intelligence Test; MRAI, Major Role Adjustment Inventory; PPI, Performance Potential Inventory; SAS-II, Social Adjustment Scale-II; BPRS, Brief Psychiatric Rating Scale

[c] Possible scores range from 0 to 50, with higher scores indicating better neurocognitive performance.

[d] Possible scores range from 0 to 100, with higher scores indicating better neurocognitive performance.

[e] Possible scores range from 0 to 20, with higher scores indicating better neurocognitive performance.

[f] Possible scores range from 1 to 19, with higher scores indicating better neurocognitive performance.

[g] Scores are given in seconds, with higher scores indicating worse neurocognitive performance.

[h] WCST 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.

[i] Possible scores range from 0 to 28, with higher scores indicating worse neurocognitive performance.

[j] Log-transformed due to skewness. Higher scores indicate better neurocognitive performance.

[k] Possible scores range from 0 to 189, with higher scores indicating worse neurocognitive performance.

[l] Possible scores range from 0 to 1, with higher scores indicating more neurological soft signs.

[m] Possible scores range from 3 to 15, with higher scores indicating greater cognitive dysfunction.

[n] Possible scores range from 9 to 45, with higher scores indicating greater impairment from cognitive dysfunction.

[o] Possible scores range from 1 to 5, with higher scores indicating worse functioning.

[p] Scores are scaled with a mean±SD of 100±50, with higher scores indicating better social-cognitive functioning.

[q] Possible scores range from 1 to 4, with higher scores indicating worse adjustment.

[r] Possible scores range from 1 to 5, with higher scores indicating better adjustment.

[s] Possible scores range from 0 to 4, with higher scores indicating worse adjustment.

[t] Possible scores range from 0 to 5, with higher scores indicating worse adjustment.

[u] Possible scores range from 1 to 7, with higher scores indicating worse adjustment.

[v] Possible scores range from 0 to 100, with higher scores indicating better adjustment.

[w] Possible scores range from 1 to 7, with higher scores indicating greater symptomatology.

[x] Possible scores range from 3 to 15, with higher scores indicating greater symptomatology.

[y] Possible scores range from 6 to 30, with higher scores indicating greater symptomatology.

Individuals receiving CET demonstrated substantial cognitive gains during the two years of treatment, particularly in social cognition, where broad social-cognitive improvements were found on multiple performance-based and clinician-rated measures. Most important, although 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. Compared with their counterparts assigned to EST, individuals in the CET group showed marked improvements in attaining competitive employment, social functioning, and global adjustment, and they showed reductions in negative symptoms. 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 (48) and remained largely unresponsive to pharmacological treatment (49). Although neurocognitive effects were moderate, it was surprising that patients with early-course schizophrenia who received CET did not show any significant improvement in processing speed, which is in contrast to our previous study with long-term patients (17). Comparison of average processing-speed scores between this early-course sample and participants in our previous study indicated that patients in the early course of their illness performed significantly better on every measure of processing speed at baseline compared with patients with chronic illness (all t values less than –2.96, all df=56, all p<.005). In fact, the pretreatment mean processing speed of individuals receiving CET in this study was comparable with that of patients with chronic illness 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 patients with early-course schizophrenic illness is not novel (6,50), 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 patients with early-course schizophrenic illness, the results of this research need to be interpreted in the context of several limitations. Our participants 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 nonspecific effects of increased clinician contact on outcome. In addition, clinicians making the assessments 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 as strong as clinician-rated measures; also, social adjustment effects were seen on an array of different measures, many of which leave little room for rater bias (employment, for example, 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 although it is possible that 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; although a hierarchical approach was used to avoid excessively inflating type I error, multiple univariate tests were conducted on within-composite measures. Finally, this research had 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, and our results indicate that our a priori power analyses based on previous studies (17) 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 included in the study to enable an adequate evaluation of the efficacy of CET in early schizophrenia. A one-year posttreatment follow-up study is being completed to ascertain the durability of these effects and to determine whether they are comparable with the sustained benefits achieved by patients with chronic schizophrenic illness (18).

Conclusions

CET is recovery-phase treatment for the remediation of social and nonsocial cognitive deficits among stable outpatients with schizophrenia. The results of this investigation suggest that the early application of CET may confer substantial benefits in cognitive functioning and broad domains of functional outcome for 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.

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