Compensatory Cognitive Training for Psychosis: Effects in a Randomized Controlled Trial

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ABSTRACT

Objective: Treatments for the cognitive impairments of schizophrenia are urgently needed. We developed and tested a 12-week, group-based, manualized, compensatory cognitive training intervention targeting prospective memory, attention, learning/memory, and executive functioning. The intervention focused on compensatory strategies, such as calendar use, self-talk, note taking, and a 6-step problem-solving method, and did not require computers.

Method: In a randomized controlled trial, 69 outpatients with *DSM-IV* primary psychotic disorders were assigned to receive standard pharmacotherapy alone or compensatory cognitive training + standard pharmacotherapy for 12 weeks. Assessments of neuropsychological performance and functional capacity (primary outcomes) and psychiatric symptom severity, quality of life, social skills performance, cognitive insight, and self-reported everyday functioning (secondary outcomes) were administered at baseline, posttreatment, and 3-month follow-up. Data were collected between September 2003 and August 2009.

Results: Hierarchical linear modeling analyses demonstrated significant compensatory cognitive training–associated effects on attention at follow-up ($P = .049$), verbal memory at posttreatment and follow-up (P values $\leq .039$), and functional capacity (University of California, San Diego Performance-based Skills Assessment) at follow-up ($P = .004$). The compensatory cognitive training group also differentially improved in negative symptom severity at posttreatment and follow-up (P values $\leq .025$) and subjective quality of life at follow-up ($P = .002$).

Conclusions: Compensatory cognitive training, a low-tech, brief intervention, has the potential to improve not only cognitive performance but also functional skills, negative symptoms, and self-rated quality of life in people with psychosis.

Trial Registration: ClinicalTrials.gov identifier: NCT01521026

J Clin Psychiatry 2012;73(9):1212–1219

Submitted: *January 30, 2012; accepted April 26, 2012.*
Online ahead of print: *August 7, 2012 (doi:10.4088/JCP.12m07686).*
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Empirically supported treatments for schizophrenia and primary psychotic disorders include a variety of psychosocial interventions, such as social skills training, supported employment, and cognitive-behavioral therapy.[1] As awareness of the functional importance of neurocognitive impairments in schizophrenia has increased,[2,3] interest in pharmacologic and behavioral treatments to improve cognition has grown. One such treatment, cognitive remediation or cognitive training, is defined as "a behavioral, training-based intervention that aims to improve cognitive processes (attention, memory, executive function, social cognition, or metacognition) with the goal of durability and generalization."[4(p472)]

The most recent meta-analysis[4] of cognitive remediation found small-to-moderate effects on cognitive tests, as well as psychosocial functioning and psychiatric symptom severity (effect sizes of 0.45, 0.42, and 0.18, respectively). There were no differences in effect sizes depending on intervention approach (strategy coaching vs drill and practice), duration of treatment, or use of computers. Most commercially available interventions, however, use computerized drill and practice exercises. Furthermore, some of the effects of these interventions may be attributable to nonspecific cognitive stimulation, as one well-controlled study found considerable cognitive improvements in a control group receiving training on computer software packages.[5] Interventions emphasizing compensatory strategies (with or without computerized drills) have produced some of the largest effect sizes in the field[6] but are less commonly used.

Our goal was to create and pilot test a cognitive training intervention that would be brief, practical, low-tech, engaging to clients, and portable enough to be delivered in the community. Accordingly, we tested the efficacy of a 12-week, manualized compensatory cognitive training intervention designed to target 4 cognitive domains: (1) prospective memory, (2) attention and vigilance, (3) learning and memory, and (4) executive functioning. These domains were selected based on their degree of impairment in schizophrenia spectrum disorders, relevance for psychosocial functioning, and potential modifiability.[2,7,8] Although prospective memory (the ability to remember to do things) generally has not been targeted in cognitive training, it predicts functional capacity,[9] treatment attendance, and adherence.[10] Our goal was to take advantage of intact abilities in schizophrenia, such as habit learning[11,12] and imagery,[13] to bolster impaired functions. Because habit learning is also highly resistant to forgetting,[14] we aimed to help participants form new habits in attention, learning, and problem-solving to automate tasks and reduce the active cognitive effort usually demanded for effective performance.

The compensatory cognitive training manual incorporated ideas and materials from various sources. The prospective memory module adapted techniques regarding external aids from the Acquired Brain Injury program at Mesa College in San Diego, California. The attention and vigilance module adapted conversational vigilance skills from Bellack and colleagues' social skills training manual[15]; the use of self-talk to improve task vigilance was informed by Meichenbaum and Cameron's work.[16] The executive functioning module included categorization tasks adapted from Delahunty and Morice's manual,[17] which Wykes and colleagues[18]

Clinical Points

- Compensatory cognitive training is a brief, manualized, low-tech intervention aimed at improving cognitive impairment and everyday functioning abilities in people with schizophrenia.
- Our results showed that compensatory cognitive training led to improvements in attention, memory, functional capacity, negative symptom severity, and patient-rated quality of life.

Table 1. Domains and Strategies Included in Compensatory Cognitive Training

Prospective memory	Calendar use; to-do lists; prioritizing tasks; linking tasks by using planned cues; automatic places; using routines to automate tasks
Attention and vigilance	Eye contact, paraphrasing, asking questions during conversations; self-talk during tasks; taking breaks to refocus
Learning and memory	Taking notes; association; chunking; categorization; acronyms; visual imagery; overlearning
Executive functioning	Six-step problem-solving method; self-talk and self-monitoring while solving problems; hypothesis testing using pro and con evidence; set shifting; set maintenance

have also used. Finally, a 6-step problem-solving method was adapted from the social skills training approach of Bellack and colleagues,[15] from which we also adapted the homework sheets for the manual. Multiple stakeholders (eg, consumers, caregivers, treating clinicians, and cognitive training experts) provided feedback during the development of the compensatory cognitive training manual (eg, participants requested assistance with remembering people's names, so a name-learning section was added). The compensatory cognitive training strategies included approaches that were both internal and external to the individual (Table 1).

Because our primary goals were to improve cognition and community functioning, our primary outcome measures were cognitive tests in the 4 targeted domains and a performance-based test of functional capacity, the University of California, San Diego (UCSD) Performance-based Skills Assessment (a common co-primary outcome measure in cognitive treatment trials).[19,20] We hypothesized that, compared to individuals receiving standard pharmacotherapy alone, participants who received the compensatory cognitive training intervention plus standard pharmacotherapy would show improvements in targeted cognitive domains and functional capacity. We also explored generalization of effects to psychiatric symptom severity, social skills performance, cognitive insight, and self-reports of cognitive problems, strategy use, everyday functioning, and quality of life.

METHOD

Participants

Participants initially enrolled in the study included 89 community-dwelling outpatients. Inclusion criteria were primary psychotic disorder (including *DSM-IV* schizophrenia, schizoaffective disorder, psychotic mood disorder, or psychosis not otherwise specified), age 18 years or older, and fluency in English. Exclusion criteria were dementia, neurologic conditions affecting cognition, mental retardation, substance use disorder within the past month, and participation in other intervention trials. The study was approved by the UCSD Institutional Review Board; all participants provided written informed consent to participate in the study. Sample characteristics and tests for differences between groups are presented in Table 2. The study was registered on ClinicalTrials.gov (identifier: NCT01521026).

Sixty-nine participants completed baseline assessments and were randomized, and 51 of these participants completed the study. Our statistical models included data from the 69 participants with a baseline assessment who were randomized; thus, we present the characteristics of these 69 participants in Table 2. Study completers (n = 51) included 23 compensatory cognitive training participants and 28 standard pharmacotherapy participants who had follow-up data. Compared to the participants who dropped out with no compensatory cognitive training exposure (n = 28), study completers (n = 51) had more education and lower daily doses of antipsychotics, but did not otherwise differ. A description of the development of the compensatory cognitive training intervention and effect sizes based on data from 38 of the 51 completers were published previously,[21] but inferential statistics have not been published.

Attrition from the study (see Supplementary eFigure 1 at PSYCHIATRIST.COM) occurred after enrollment but before baseline assessment (n = 14), after baseline assessment but before randomization (n = 6), after randomization to standard pharmacotherapy (n = 3), after randomization to compensatory cognitive training but before any exposure to the compensatory cognitive training intervention (n = 5), or after randomization and attendance of at least 1 compensatory cognitive training session (n = 10). Of those who attended at least 1 compensatory cognitive training session but later dropped out, 7 attended only 1 session and 1 person each attended 2, 5, and 10 sessions (thus, these 10 participants attended an average of 2.4 sessions). Common reasons for dropping out of the compensatory cognitive training intervention or the study itself were being too busy or not wanting treatment for cognitive impairment, but most dropouts simply could not be contacted. Those assigned to compensatory cognitive training who did not drop out attended an average of 10.6 of 12 compensatory cognitive training sessions (range, 6–12). There were no significant differences between participants who completed compensatory cognitive training and those who began compensatory cognitive training but later dropped out.

Procedure

Data were collected between September 2003 and August 2009. Participants were referred to the study by treating clinicians or self-referral. Compensatory cognitive training was described to potential participants as a thinking and memory "class" to destigmatize the focus on cognitive impairment

Table 2. Baseline Group Comparison of Randomized Participants (n = 69)

Variable	Compensatory Cognitive Training n	Compensatory Cognitive Training Value	Standard Pharmacotherapy n	Standard Pharmacotherapy Value	t or χ^2	P Value[a]
Demographics						
Age, mean (SD), y	38	44.3 (10.1)	31	48.8 (8.7)	1.98	.052
Male gender, %	38	63.2	31	67.7	0.16	.691
Education, mean (SD), y	38	12.9 (1.8)	31	13.0 (1.6)	0.39	.697
White race/ethnicity, %	38	63.2	31	54.8	0.49	.484
Housing, living independently, %	37	81.1	30	80.0	0.38	.539
Marital status, ever married, %	38	42.1	30	46.7	0.14	.707
Illness burden						
Diagnosis, %					2.09	.554
Schizophrenia	20	52.6	17	54.8		
Schizoaffective disorder	17	44.7	13	41.9		
Psychosis not otherwise specified	1	2.6	0	0.0		
MDD with psychotic features	0	0.0	1	3.2		
Illness duration, mean (SD), y	38	21.1 (13.5)	31	25.9 (10.3)	1.64	.107
Antipsychotic medication type, %					2.73	.435
None	1	2.8	3	9.7		
Typical	1	2.8	2	6.5		
Atypical	33	91.7	24	77.4		
Both	1	2.8	2	6.5		
Chlorpromazine equivalent dose, mean (SD), mg	29	479.37 (455.07)	28	266.67 (246.49)	2.20	**.033**
Clinical/functioning measures, mean (SD)						
PANSS positive symptoms score	38	16.26 (6.58)	31	17.16 (6.12)	0.58	.563
PANSS negative symptoms score	38	15.66 (6.24)	31	14.23 (4.90)	1.07	.290
HDRS score (depressive symptoms)	38	12.00 (7.45)	29	11.34 (6.37)	0.38	.706
UPSA score (functional capacity)	38	82.44 (9.90)	30	85.47 (8.42)	1.33	.187
SSPA score (social skills performance)	38	31.25 (6.24)	31	31.13 (6.06)	0.08	.936
QOLI score (subjective quality of life)	37	4.16 (1.59)	30	4.43 (1.38)	0.74	.465
CPSA score (cognitive problems)	38	1.14 (0.52)	30	0.92 (0.42)	1.87	.066
CPSA score (cognitive strategies)	38	1.31 (0.43)	30	1.43 (0.44)	1.10	.275
Neuropsychological raw scores						
Premorbid IQ estimate	36	106.42 (9.66)	31	107.55 (10.40)	0.46	.646
Targeted domains						
Prospective memory (MIST total)	38	28.82 (11.74)	31	29.71 (9.08)	0.36	.723
Attention (maximum forward Digit Span)	38	6.08 (1.36)	31	6.23 (1.59)	0.41	.680
Verbal learning (HVLT-R recall total)	38	24.63 (5.94)	31	22.87 (5.44)	1.27	.208
Verbal memory (HVLT-R percentage retained)	38	86.12 (14.95)	31	90.94 (19.71)	1.16	.252
Executive functioning (WCST total)	37	42.84 (9.72)	31	40.97 (12.79)	0.67	.507
Nontargeted domains						
Processing speed (Digit Symbol total)	38	52.03 (15.37)	31	52.71 (13.26)	0.20	.846
Working memory (LNS total)	38	8.32 (2.57)	31	8.39 (2.56)	0.11	.909
Verbal fluency (COWAT total)	37	41.3 (11.45)	31	41.65 (11.02)	0.13	.899

[a]Bold font indicates significant difference.

Abbreviations: COWAT = Controlled Oral Word Association Test; CPSA = Cognitive Problems and Strategies Assessment; HDRS = Hamilton Depression Rating Scale; HVLT-R = Hopkins Verbal Learning Test-Revised; LNS = Letter-Number Sequencing; MDD = major depressive disorder; MIST = Memory for Intentions Screening Test; PANSS = Positive and Negative Syndrome Scale; QOLI = Quality of Life Interview; SSPA = Social Skills Performance Assessment; UPSA = University of California, San Diego Performance-Based Skills Assessment; WCST = Wisconsin Card Sorting Test.

and to emphasize skill acquisition rather than psychotherapy. Diagnoses were confirmed via *DSM-IV*–based diagnostic chart reviews and/or structured diagnostic interview (Mini-International Neuropsychiatric Interview).[22] Following baseline assessment, participants were randomly assigned to receive compensatory cognitive training plus standard pharmacotherapy (compensatory cognitive training) or standard pharmacotherapy alone. Early in the study, randomization occurred following each participant's baseline assessment, but, to save time, we altered the study procedure to randomize in blocks of 5, meaning that, after 5 participants were enrolled and completed baseline assessment, they were randomized as a group to receive either compensatory cognitive training or standard pharmacotherapy.

The compensatory cognitive training intervention was delivered in groups in 12, 2-hour sessions over 12 weeks in 2 community-based mental health clinics that followed a psychosocial rehabilitation model.[1] The compensatory cognitive training groups consisted of 5 participants and 2 therapists; therapists were E.W.T. and doctoral trainees trained and supervised by E.W.T. The structure of the compensatory cognitive training intervention was determined by the treatment manual but was also intended to be interactive and personally meaningful to the participants. Sessions included a review of homework, troubleshooting of strategy use, psychoeducation and rationale for the targeted domains, demonstration and practice of each strategy, feedback on strategy use, and individualized discussion regarding implementation of the

strategies in daily life. A break was provided between the first and second hours of each session. Homework was assigned to encourage real-world implementation of strategies as well as to provide an opportunity to troubleshoot any difficulties. Compensatory cognitive training did not use computers, and strategies taught did not "train to the test" or use any of the outcome measures during training. Therapists and participants all used the treatment manual during sessions.

Participants completed outcome assessments at post-treatment and at 3-month follow-up. Personnel performing the assessments were blind to group assignment and trained to a high level of reliability on symptom rating instruments (intraclass correlation coefficient ≥ 0.80). Participants were compensated for their time and travel to assessment sessions, but they were not paid for attending compensatory cognitive training sessions. Chlorpromazine equivalent amounts in milligrams were used to convert antipsychotic medication dosages at baseline according to standard formulas (except clozapine and injectables).[23,24]

Measures

Neuropsychological measures included an estimate of premorbid intellectual functioning, the American National Adult Reading Test.[25] Additional neuropsychological measures of domains targeted by the compensatory cognitive training strategies included (1) prospective memory (Memory for Intentions Screening Test[26] [total score]), (2) attention (Wechsler Adult Intelligence Scale, third edition [WAIS-III][27] Digit Span forward maximum span [isolated from Digit Span backward to measure attention rather than working memory, which was not targeted in compensatory cognitive training]), (3) verbal learning and memory (Hopkins Verbal Learning Test-Revised[28] [total immediate recall and percentage retained]), and (4) executive functioning (Wisconsin Card Sorting Test[29] [total correct]).

The nontargeted domains were measured as follows: (1) processing speed (WAIS-III Digit Symbol[27] [total correct]), (2) working memory (WAIS-III Letter-Number Sequencing[27] [total correct]), and (3) verbal fluency (Controlled Oral Word Association Test[30] [animals/fruits/vegetables total]).

Functional capacity was measured with the UCSD Performance-based Skills Assessment, which uses structured role-play scenarios to measure ability in 5 everyday living domains (household chores, eg, shopping in the context of a provided recipe; communication, eg, using the telephone for emergency and routine situations; finance, eg, making change and paying a bill by check; transportation, eg, planning a bus route; and planning recreational activities, eg, planning an outing).[19] The UCSD Performance-based Skills Assessment total score (0–100) is moderately correlated with global neuropsychological functioning[31,32] but has been shown to better predict real-world outcomes such as living independence.[33]

Secondary outcomes and other assessments to characterize the sample included established measures. The Social Skills Performance Assessment,[34] a role-play test of social skills, assessed ability in the context of neutral and confrontational social scenarios. The Independent Living Skills Survey[35] was administered as a self-report measure of functioning. Psychiatric symptom severity was measured by the Positive and Negative Syndrome Scale (PANSS)[36] and the Hamilton Depression Rating Scale (HDRS).[37] Cognitive insight was measured by the Beck Cognitive Insight Scale,[38] which includes items assessing self-reflectiveness, openness to feedback, and certainty about beliefs. Quality of life was measured by the Quality of Life Interview.[39] Self-reported cognitive problems and cognitive strategy use were measured by the Cognitive Problems and Strategies Assessment (eAppendix 1).

Data Analyses

All variables were inspected for normality; no data transformations were needed. Study hypotheses were tested using hierarchical linear modeling, an intent-to-treat method using all available data points. The age of the 2 groups was close to significantly different (see Table 2); therefore, age was added to the hierarchical linear modeling analyses to test whether the group-by-time effects varied by age. Although chlorpromazine equivalent dosage was significantly different between the groups (see Table 2), it was not added to the models because it was not available for all participants due to the conversion formula restrictions. Time was modeled as a discrete parameter, as there were only 3 time points, and the baseline assessment was used as the reference time point. A random intercept for individuals was included in all models. The level 1 parameters were group (compensatory cognitive training and standard pharmacotherapy, with standard pharmacotherapy as the reference category), age (grand mean centered), and time; the level 2 parameter was individuals. For primary outcomes and for secondary outcome variables with significant hierarchical linear modeling results, Cohen *d* effect sizes were then calculated using group differences in change scores (*n*'s with complete data ranged from 42 to 48). All statistical models were computed with and without outliers. The models were also run without the subjects with primary psychotic disorders other than schizophrenia or schizoaffective disorder; the results did not change, so results from the entire sample are reported.

RESULTS

Table 3 presents all significant and borderline significant ($P = .05$) model parameter estimates and test statistics for the primary and secondary outcome measures, and Figure 1 provides graphs of these group-by-time interactions. Other models are presented in eTable 1.

Treatment Effects on Targeted Cognitive Domains

Compared to participants receiving standard pharmacotherapy, those in the compensatory cognitive training group demonstrated improvement in attention at 3-month follow-up ($P = .049$). The compensatory cognitive training group

Table 3. Hierarchical Linear Models

	Attention (maximum forward Digit Span)					Verbal Memory (HVLT-R percentage retained)					Prospective Memory (MIST total score)				
	Effect Estimate	SE	*t*	*df*	*P* Value[a]	Effect Estimate	SE	*t*	*df*	*P* Value[a]	Effect Estimate	SE	*t*	*df*	*P* Value[a]
Intercept	6.22	0.26	23.96	101.53	**<.001**	91.66	3.21	28.52	12.73	**<.001**	3.38	1.95	15.60	82.60	**<.001**
Time															
Posttreatment	0.16	0.27	0.59	92.67	.554	−6.32	3.92	−1.61	95.35	.110	1.79	1.50	1.19	86.63	.237
3-Month follow-up	−0.14	0.26	−0.53	92.14	.596	−4.38	3.80	−1.15	94.01	.253	1.74	1.45	1.20	86.30	.232
Group (CCT)	0.00	0.02	0.17	101.53	.867	-.29	0.23	−1.27	12.73	.207	−0.27	0.14	−1.96	82.60	.054
Age	−0.13	0.35	−0.38	101.53	.708	−6.13	4.39	−1.40	12.73	.164	−2.12	2.66	−0.80	82.60	.428
Age × time															
Posttreatment	0.00	0.02	0.21	97.63	.833	.51	0.30	1.69	102.19	.094	0.21	0.12	1.77	89.40	.080
3-Month follow-up	−0.02	0.02	−1.01	96.85	.317	.61	0.29	2.14	10.29	**.035**	0.26	0.11	2.30	89.24	**.024**
Group × time															
Posttreatment	0.38	0.39	0.98	96.67	.330	13.76	5.69	2.42	10.71	**.017**	1.75	2.22	0.79	88.91	.431
3-Month follow-up	0.75	0.38	1.99	96.20	**.049**	11.53	5.51	2.09	99.59	**.039**	4.25	2.13	1.99	88.75	**.050**

	Functional Capacity (UPSA total score)					Negative Symptom Severity (PANSS)					Subjective Quality of Life (QOLI)				
	Effect Estimate	SE	*t*	*df*	*P* Value[a]	Effect Estimate	SE	*t*	*df*	*P* Value[a]	Effect Estimate	SE	*t*	*df*	*P* Value[a]
Intercept	85.40	1.64	52.16	95.51	**<.001**	13.89	1.04	13.33	98.16	**<.001**	4.50	0.27	16.43	92.56	**<.001**
Time															
Posttreatment	−0.90	1.58	−0.57	88.49	.569	2.16	0.98	2.19	94.39	**.031**	0.01	0.26	0.03	87.65	.977
3-Month follow-up	−1.48	1.52	−0.97	88.75	.335	2.75	0.96	2.86	94.02	**.005**	−0.42	0.25	−1.68	87.92	.096
Group (CCT)	−0.07	0.11	−0.58	93.90	.563	0.13	0.07	1.82	98.16	.073	−0.04	0.02	−2.00	91.00	**.048**
Age	−3.09	2.22	−1.39	94.50	.168	2.04	1.42	1.43	98.16	.155	−0.42	0.38	−1.13	91.56	.260
Age × time															
Posttreatment	−0.01	0.12	−0.10	92.84	.918	−0.04	0.08	−0.58	98.40	.560	0.02	0.02	0.81	91.66	.422
3-Month follow-up	0.23	0.11	1.99	92.34	.050	−0.16	0.07	−2.20	97.94	**.030**	0.04	0.02	2.00	91.19	**.049**
Group × time															
Posttreatment	3.12	2.31	1.35	92.21	.181	−4.57	1.44	−3.18	97.68	**.002**	0.52	0.38	1.36	9.94	.176
3-Month follow-up	6.57	2.21	2.97	92.15	**.004**	−3.23	1.42	−2.28	97.51	**.025**	1.15	0.36	3.17	9.87	**.002**

[a]Bold font indicates significant difference.

Abbreviations: CCT = compensatory cognitive training; HVLT-R = Hopkins Verbal Learning Test-Revised; MIST = Memory for Intentions Screening Test; PANSS = Positive and Negative Syndrome Scale; QOLI = Quality of Life Interview; SE = standard error; UPSA = University of California, San Diego Performance-Based Skills Assessment.

differentially improved in verbal memory at both posttreatment and 3-month follow-up (*P* values ≤ .039). Group differences at the 3-month follow-up approached significance for prospective memory (*P* = .05), with the compensatory cognitive training group showing more improvement than the standard pharmacotherapy group.

Treatment Effects on Functional Capacity

Compared with those in the standard pharmacotherapy group, participants in the compensatory cognitive training intervention improved significantly more in functional capacity (UCSD Performance-based Skills Assessment) at the 3-month follow-up time point (*P* = .004).

Treatment Effects on Other Secondary Outcomes

There were also compensatory cognitive training–associated improvements in negative symptoms at posttreatment and 3-month follow-up (*P* values ≤ .025) and in subjective quality of life at the 3-month follow-up (*P* = .002).

Treatment Effects on Self-Reported Cognitive Problems and Strategy Use

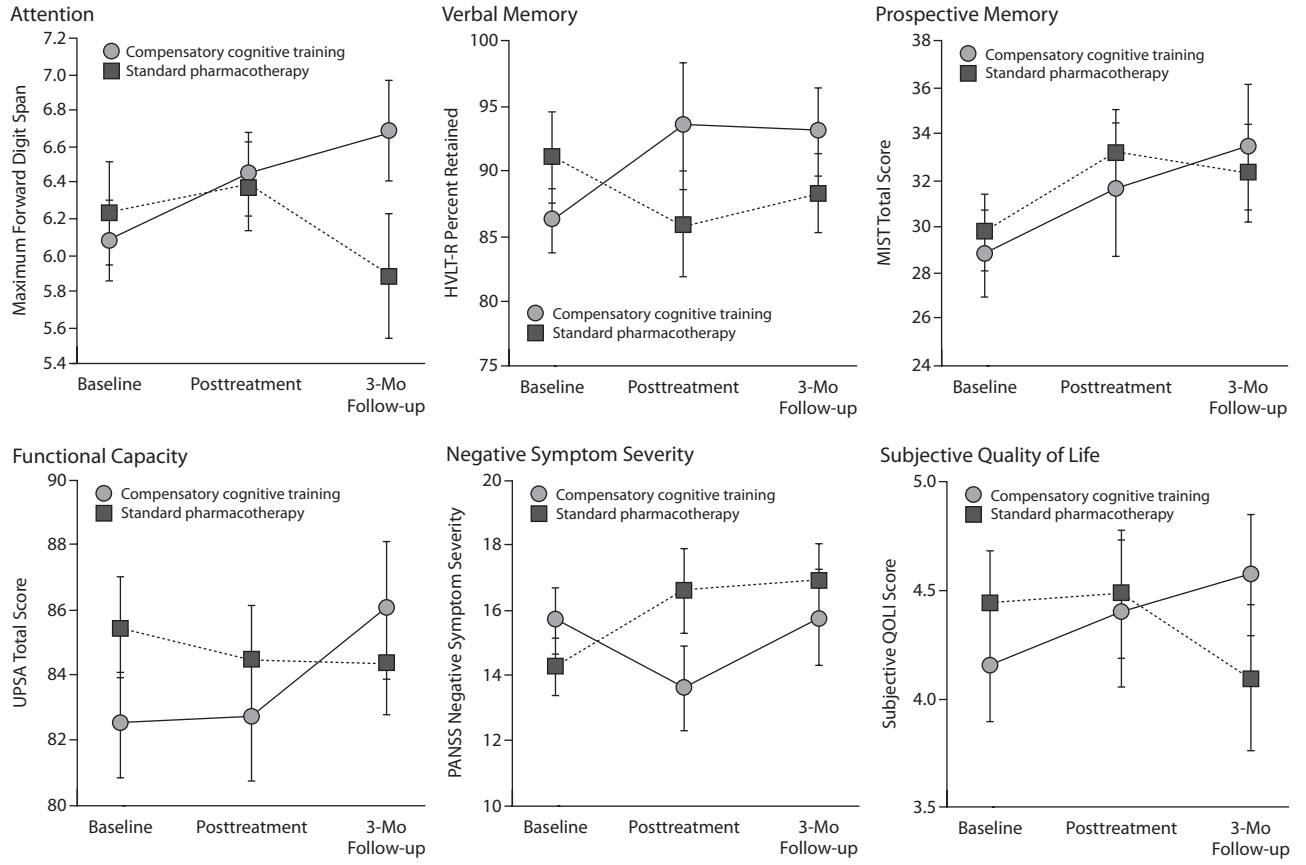
Compensatory cognitive training participants reported significantly fewer cognitive problems than did standard pharmacotherapy participants at posttreatment (effect estimate = −0.24, standard error [SE] = 0.10, *P* = .020), and those in the compensatory cognitive training group reported using more cognitive strategies than did standard pharmacotherapy participants at both posttreatment (effect estimate = 0.47, SE = 0.13, *P* < .001) and follow-up (effect estimate = 0.40, SE = 0.20, *P* = .002).

All other group differences in outcomes at posttreatment and follow-up were nonsignificant (*P* values ≥ .158), and the group-by-time effects did not vary by age for any outcomes (*P* values ≥ .121). Effect sizes comparing the groups' change scores at posttreatment and 3-month follow-up for all outcome measures are presented in Table 4.

Sensitivity Analysis

The following variables were found to have outliers > 1.5 times the interquartile range: Hopkins Verbal Learning Test-Revised percentage retained, Digit Symbol total correct, Letter-Number Sequencing total correct, PANSS negative symptoms, HDRS, UCSD Performance-based Skills Assessment, and Cognitive Problems and Strategies Assessment cognitive problems. Sensitivity analyses were run excluding the outliers for each of the above variables. When outliers were removed, the group difference was no longer significant at the posttreatment time point for verbal memory (*P* = .078); however, the group difference at follow-up remained significant (effect estimate = −11.49, SE = 5.17, *P* = .029). The group difference in self-reported cognitive problems at posttreatment also became nonsignificant (*P* = .070) when the outliers

Figure 1. Mean (SD) Values of Outcomes by Group



Abbreviations: HVLT-R = Hopkins Verbal Learning Test-Revised; MIST = Memory for Intentions Screening Test; PANSS = Positive and Negative Syndrome Scale; QOLI = Quality of Life Interview; UPSA = University of California, San Diego Performance-based Skills Assessment.

were removed. The findings for all of the other outcomes tested did not change.

DISCUSSION

Our results showed that, compared with participants receiving standard pharmacotherapy alone, those who received group compensatory cognitive training plus standard pharmacotherapy for 12 weeks demonstrated improvements in some targeted areas of cognition (attention and memory; $P = .05$ trend for prospective memory), functional capacity as measured by the UCSD Performance-based Skills Assessment, negative symptom severity, and subjective quality of life. Effect sizes associated with significant cognitive improvements ranged from small to medium (0.24–0.53). However, the effect sizes associated with significant improvement in functional capacity (0.61), negative symptom severity (0.92), and subjective quality of life (0.81) were larger. It may be that compensatory cognitive training and similar interventions have small-to-moderate cognitive effects that can, in turn, yield larger effects in more distal functional outcomes, or it may be that compensatory cognitive training had effects on symptoms or functioning that were independent of cognitive improvement. Many of the effect sizes associated with compensatory cognitive training exceeded the average effect size benchmarks in published trials to date (ie, 0.45 for cognition, 0.42 for psychosocial functioning, and 0.18 for symptoms, according to the recent meta-analysis by Wykes and colleagues[4]), despite compensatory cognitive training being a briefer than average intervention (24 hours vs 32 hours).[4]

Importantly, some effect sizes increased from posttreatment to 3-month follow-up (ie, those for prospective memory, attention, learning, executive functioning, functional capacity, and subjective quality of life), which may result from continued strategy practice during the follow-up period. However, the improvements in negative symptom severity and self-rated cognitive problems were smaller at 3-month follow-up than at posttreatment. Improvements in negative symptom severity following cognitive remediation are not unusual,[6,40,41] but little is known about the time course of such improvements. In the case of compensatory cognitive training, it is possible that group participation had a salutary effect on negative symptoms, but the effect was attenuated during the follow-up period. Similarly, participation in compensatory cognitive training may have heightened participants' awareness of cognitive problems, but such awareness may have diminished during the follow-up period. Finally, although compensatory cognitive training's effects on attention and subjective quality of life showed continued improvement at 3-month follow-up, the

Table 4. Effect Sizes for Group Differences in Change Scores at Posttreatment and 3-Month Follow-Up[a]

Variable	Posttreatment Minus Baseline Change Score	3-Month Follow-Up Minus Baseline Change Score
Targeted cognitive domain		
Prospective memory (MIST total)	0.09	0.53
Attention (maximum forward Digit Span)	0.10	0.24
Verbal learning (HVLT-R recall total)	0.03	0.27
Verbal memory (HVLT-R % retained)	0.53	0.38
Executive functioning (WCST total)	0.23	0.34
Nontargeted cognitive domains		
Processing speed (Digit Symbol total)	−0.05	0.02
Working memory (LNS total)	−0.13	0.03
Verbal fluency (COWAT total)	0.11	0.06
Functional capacity (UPSA)	0.61	0.72
Social skills performance (SSPA)	0.06	0.14
Negative symptoms (PANSS)	0.92	0.43
Positive symptoms (PANSS)	0.03	0.27
Depressive symptoms (HDRS)	0.14	0.19
Subjective quality of life (QOLI)	0.53	0.81
CPSA cognitive problems	0.88	0.46
CPSA cognitive strategies	0.85	0.84

[a]All effect sizes have been presented such that a positive effect size denotes differential improvement in the compensatory cognitive training group compared with the standard pharmacotherapy group.
Abbreviations: COWAT = Controlled Oral Word Association Test; CPSA = Cognitive Problems and Strategies Assessment; HDRS = Hamilton Depression Rating Scale; HVLT-R = Hopkins Verbal Learning Test-Revised; LNS = Letter-Number Sequencing; MIST = Memory for Intentions Screening Test; PANSS = Positive and Negative Syndrome Scale; QOLI = Quality of Life Interview; SSPA = Social Skills Performance Assessment; UPSA = University of California, San Diego Performance-based Skills Assessment; WCST = Wisconsin Card Sorting Test.

significance of these effects may have been partially attributable to declining scores in the standard pharmacotherapy group.

Although our initial results are promising, this study has limitations, including a small sample size and a relatively short follow-up period. We also had a significant dropout rate and have presented results related to predictors of dropout in a separate publication[42] (briefly, we found that study completers had more formal education and lower daily doses of antipsychotic medications than did dropouts with no compensatory cognitive training exposure, and there were no significant differences between participants who completed compensatory cognitive training and those who began compensatory cognitive training but later dropped out). Because compensatory cognitive training is a novel intervention and our primary research question concerned its efficacy, we did not use an active control condition that matched compensatory cognitive training for therapist time or group involvement; our results should be considered preliminary until they are replicated in a larger sample in a study using an active control condition. Although we do not believe that the effects of compensatory cognitive training on objective neuropsychological and performance-based functioning tests administered by blinded raters to be attributable to nonspecific therapeutic factors, such factors could have affected self-report measures (eg, quality of life). A new study of compensatory cognitive training using a robust control group is now underway. Although compensatory cognitive training participants reported using the strategies they were taught, we did not collect data on homework completion, nor did we have an objective measure of strategy use in real-world settings. We did not correct for α inflation due to our small sample size, and it is possible that some of our results reflect type I error. On the other hand, our pilot study was adequately powered (0.80) to detect large ($d = 0.8$) effect sizes, and the consistency of the findings supports the conclusion regarding significant benefits of compensatory cognitive training in this population. Also, although compensatory cognitive training was delivered in clinics that offered psychosocial rehabilitation opportunities, not all clients participated in rehabilitation activities, and, as a research-based group, compensatory cognitive training was not well integrated with other treatment or rehabilitation options. Previous meta-analyses[4,43] have shown that cognitive remediation is more effective when integrated within a broader psychiatric rehabilitation program, such as one that includes supported employment.[44,45] It is possible that the effects of compensatory cognitive training could have been greater in the context of psychiatric rehabilitation.

In summary, these preliminary results lead us to recommend further research on compensatory cognitive training and similar interventions for people with psychosis. Future measurement of motivation and insight regarding neurocognitive impairment could result in better clinical tailoring of cognitive remediation interventions to specific individuals.[46–48] Just as some restorative cognitive remediation approaches have shown effects on brain structure, function, and biomarkers such as brain-derived neurotrophic factor,[49–51] it is possible that the behavior changes resulting from compensatory cognitive remediation interventions could result in observable brain changes, which should be measured in future investigations.

Drug names: clozapine (Clozaril, FazaClo, and others).
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Potential conflicts of interest: All authors report no competing interests.
Funding/support: Funding for this study was provided by grants from the National Alliance for Research on Schizophrenia and Depression and by the National Institute of Mental Health (R01MH080150, P30MH080002, and R34MH93453).
Previous presentation: An early version of this work was presented at the Schizophrenia International Research Society Annual Meeting; April 10–14, 2010; Florence, Italy.
Supplementary material: Available at PSYCHIATRIST.COM.

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THE JOURNAL OF CLINICAL PSYCHIATRY

Supplementary Material

Article Title: Compensatory Cognitive Training for Psychosis: Effects in a Randomized Controlled Trial

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DOI Number: 10.4088/JCP.12m07686

List of Supplementary Material for the article

1. **eFigure 1** CONSORT Diagram
2. **eTable 1** Hierarchical Linear Models
3. **eAppendix 1** Cognitive Problems and Strategies Assessment

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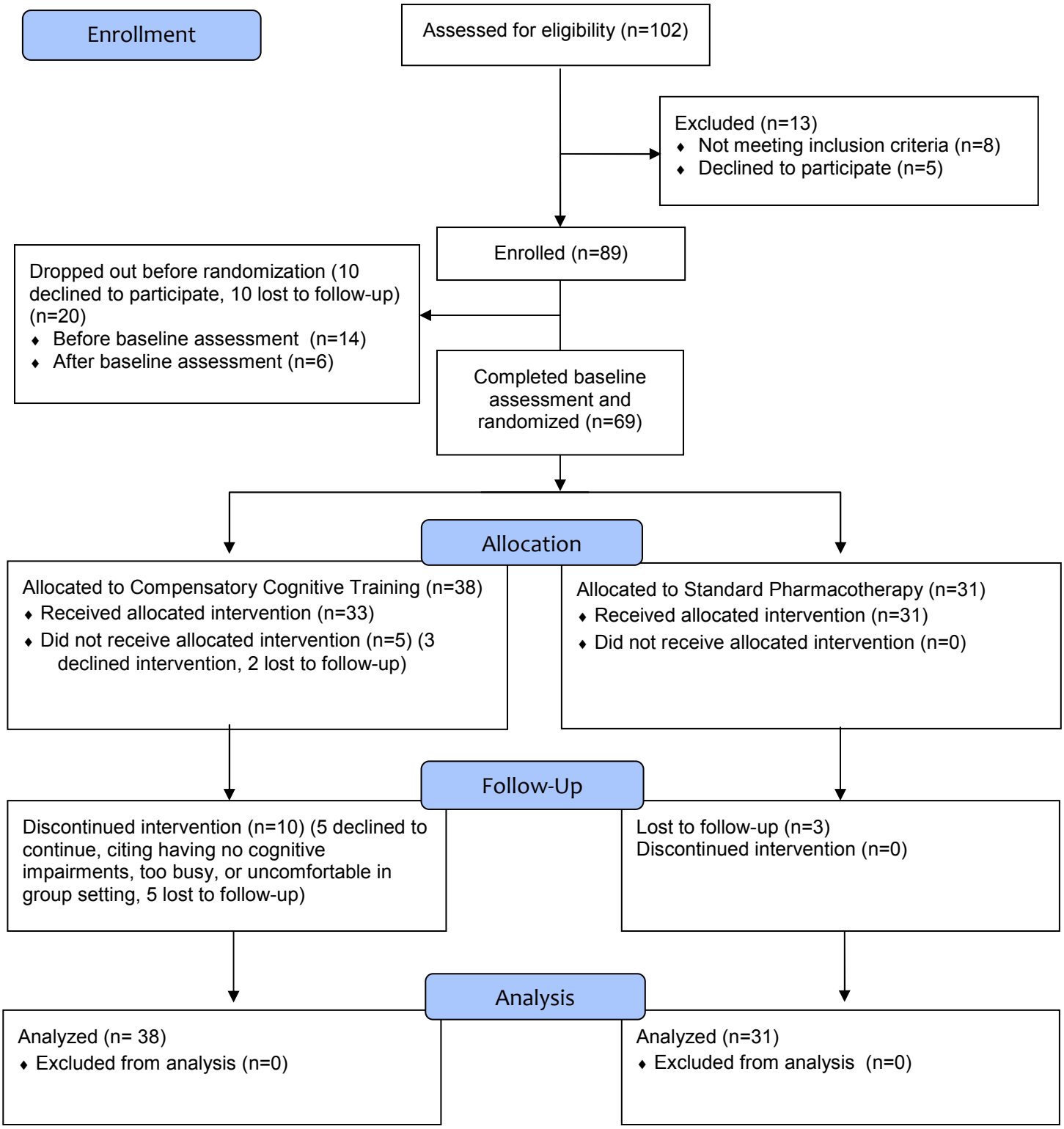
eFigure 1. CONSORT Diagram



eTable 1. Hierarchical Linear Models

	Verbal Learning (HVLT-R recall total)					Executive Functioning (WCST total)					Processing Speed (Digit Symbol total)				
	EE	**SE**	**t**	**df**	**p-value**	**EE**	**SE**	**t**	**df**	**p-value**	**EE**	**SE**	**t**	**df**	**p-value**
Intercept	22.97	1.07	21.42	103.82	**<0.001**	40.91	2.03	20.14	89.53	**<0.001**	53.43	2.53	21.16	78.15	**<0.001**
Visit															
Post-treatment	1.28	1.11	1.15	95.09	0.251	-1.89	1.89	-1.00	89.55	0.319	-1.40	1.62	-0.86	89.54	0.391
3 Month Follow-up	0.83	1.08	0.77	94.32	0.441	1.06	1.82	0.58	89.12	0.563	-2.48	1.57	-1.58	89.33	0.118
Group (CCT)	-0.04	0.08	-0.54	103.82	0.590	0.02	0.15	0.16	89.53	0.876	-0.29	0.18	-1.62	78.15	0.109
Age	1.57	1.46	1.08	103.82	0.284	1.96	2.77	0.71	89.53	0.481	-2.00	3.45	-0.58	78.15	0.564
Age*Visit															
Post Treatment	0.00	0.09	-0.03	100.13	0.978	0.20	0.14	1.37	91.02	0.176	0.03	0.13	0.24	91.52	0.810
3 Month Follow-up	0.05	0.08	0.63	99.23	0.530	-0.11	0.14	-0.78	90.46	0.438	0.10	0.12	0.79	91.39	0.431
Group*Visit															
Post-treatment	-0.22	1.63	-0.14	99.16	0.892	3.87	2.71	1.42	91.75	0.158	-0.63	2.39	-0.26	91.20	0.792
3 Month Follow-up	1.44	1.57	0.91	98.61	0.363	3.04	2.62	1.16	91.48	0.249	1.21	2.31	0.52	91.10	0.602

	Working Memory (LNS total)					Verbal Fluency (COWAT total)				
	EE	**SE**	**t**	**df**	**p-value**	**EE**	**SE**	**t**	**df**	**p-value**
Intercept	8.31	0.49	16.89	82.70	**<0.001**	41.86	2.00	20.89	79.12	**<0.001**
Visit										
Post-treatment	-0.02	0.37	-0.06	90.21	0.951	0.63	1.42	0.44	89.19	0.657
3 Month Follow-up	0.00	0.36	0.00	89.90	0.998	-0.65	1.38	-0.47	88.92	0.636
Group (CCT)	0.03	0.03	0.93	82.70	0.353	-0.09	0.14	-0.60	79.12	0.549
Age	0.08	0.67	0.11	82.70	0.910	-0.72	2.74	-0.26	79.12	0.793
Age*Visit										
Post Treatment	-0.01	0.03	-0.43	92.93	0.667	-0.13	0.11	-1.13	91.56	0.262
3 Month Follow-up	-0.04	0.03	-1.48	92.69	0.143	0.09	0.11	0.84	91.36	0.404
Group*Visit										
Post-treatment	-0.19	0.54	-0.35	92.46	0.726	0.07	2.10	0.03	91.13	0.974
3 Month Follow-up	-0.04	0.53	-0.07	92.30	0.946	1.06	2.03	0.52	90.99	0.601

	Positive Symptom Severity (PANSS)					Depressive Symptoms (HAM-D)					Social Skills Performance (SSPA)				
	EE	**SE**	**t**	**df**	**p-value**	**EE**	**SE**	**t**	**df**	**p-value**	**EE**	**SE**	**t**	**df**	**p-value**
Intercept	17.28	1.12	15.43	95.55	**<0.001**	11.50	1.29	8.90	87.54	**<0.001**	31.04	1.18	26.35	101.44	**<0.001**
Visit															
Post-treatment	-0.87	1.07	-0.81	91.62	0.418	-0.99	1.14	-0.86	84.67	0.390	-0.52	1.19	-0.44	95.00	0.664
3 Month Follow-up	0.19	1.04	0.18	91.00	0.854	1.42	1.12	1.27	84.33	0.209	-0.90	1.14	-0.78	94.05	0.435

Group (CCT)	-0.05	0.08	-0.62	95.55	0.535	-0.03	0.09	-0.31	85.53	0.755	0.04	0.08	0.43	101.44	0.667
Age	-1.12	1.53	-0.73	95.55	0.465	0.45	1.74	0.26	86.64	0.799	0.28	1.61	0.18	101.44	0.860
Age*Visit															
Post Treatment	0.04	0.08	0.50	95.91	0.616	-0.01	0.09	-0.10	87.92	0.920	-0.03	0.09	-0.38	99.35	0.705
3 Month Follow-up	-0.04	0.08	-0.56	95.38	0.580	-0.16	0.08	-1.86	87.54	0.067	-0.02	0.09	-0.24	98.59	0.813
Group*Visit															
Post-treatment	-0.27	1.57	-0.17	95.13	0.862	-0.48	1.66	-0.29	87.45	0.775	0.50	1.73	0.29	98.56	0.774
3 Month Follow-up	-1.55	1.54	-1.01	94.90	0.316	-1.71	1.65	-1.03	87.39	0.305	0.87	1.67	0.52	98.01	0.604

	CPSA Cognitive Problems					**CPSA Cognitive Strategies**				
	EE	**SE**	**t**	**df**	**p-value**	**EE**	**SE**	**t**	**df**	**p-value**
Intercept	0.93	0.09	10.79	83.20	**<0.001**	1.44	0.09	16.39	102.56	**<0.001**
Visit										
Post-treatment	-0.05	0.07	-0.70	85.99	0.487	-0.02	0.09	-0.19	92.99	0.849
3 Month Follow-up	-0.10	0.07	-1.48	86.27	0.143	-0.01	0.09	-0.12	93.21	0.905
Group (CCT)	0.01	0.01	1.13	81.97	0.261	0.00	0.01	-0.56	100.97	0.579
Age	0.22	0.12	1.89	82.43	0.063	-0.14	0.12	-1.14	101.57	0.257
Age*Visit										
Post Treatment	0.00	0.01	0.60	88.85	0.547	0.01	0.01	1.39	97.59	0.168
3 Month Follow-up	0.00	0.00	0.86	88.68	0.390	0.00	0.01	0.41	96.99	0.684
Group*Visit										
Post-treatment	-0.24	0.10	-2.37	88.46	**0.020**	0.47	0.13	3.65	96.91	**0.000**
3 Month Follow-up	-0.11	0.10	-1.12	88.54	0.268	0.40	0.12	3.23	96.79	**0.002**

Note. Significant findings are indicated in bold font. CCT = Compensatory Cognitive Training; COWAT = Controlled Oral Word Association Test; CPSA = Cognitive Problems and Strategies Assessment; EE = Effect Estimate; HAM-D = Hamilton Depression Rating Scale; HVLT-R = Hopkins Verbal Learning Test-Revised; LNS = Letter-Number Sequencing; PANSS = Positive and Negative Syndrome Scale; SE = Standard Error; SSPA = Social Skills Performance Assessment; WCST = Wisconsin Card Sorting Test

eAppendix 1. Cognitive Problems and Strategies Assessment

Please read the subject item and record the response by placing a check in the appropriate box.

Say, "First I'm going to ask you about problems some people have with their thinking and memory. Tell me how frequently each one is a problem for you, using this scale." Show the subject the scale (detach the back page).

Problems With Thinking and Memory

	Rarely/ Never (0)	Sometimes (1)	Often (2)	Always (3)
1. I have difficulty remembering to do things that I have scheduled.				
2. I forget to go to doctor's appointments.				
3. I have difficulty remembering to take medications.				
4. I forget to do housework or chores.				
5. I have difficulty remembering to take a bath or shower.				
6. I forget whether I've taken my medication.				
7. I have trouble remembering events that are coming up in the next few weeks.				
8. I forget people's names.				
9. I have trouble remembering the names of my medications.				
10. I forget my medication dosages.				
11. I have difficulty memorizing things that I need to know.				
12. I forget details from conversations.				
13. I have problems with memory retrieval (I know the information is in my brain, but I just can't seem to get it out).				
14. I have trouble learning new information.				
15. I lose things like my keys, glasses, or wallet.				
16. If I have a lot of things to do, I have trouble knowing which thing to do first.				
17. My living space is a mess because I have trouble getting organized with my chores.				
18. I run out of medication because I have not planned ahead to get my medication.				
19. I have trouble staying focused during conversations.				
20. I get distracted by other things when I am talking with someone.				
21. I have trouble staying focused while I work on a task.				
22. I get distracted by other things when				

I am working on a project.				
23. When I have a conversation, I got off track instead of staying on the topic.				
24. When I don't understand what someone is saying, I just pretend that I do understand.				
25. I have trouble understanding what to do when someone gives me instructions.				
26. I have trouble solving problems.				
27. My thinking gets stuck in a rut.				
28. When I need to solve a problem, I try one solution, and if it doesn't work, I give up.				
29. There is only one way to solve a problem.				
30. If I'm solving a problem and my solution is not working, I keep trying the same strategy until it works.				

Say, “Now I’m going to ask you about strategies some people use to help with their thinking and memory. Tell me how frequently you use each one, using the same scale.”

Memory and Thinking Strategies

	Rarely/ Never (0)	Sometimes (1)	Often (2)	Always (3)
1. I use a calendar regularly to schedule and remember appointments and activities.				
2. I check a calendar every day to see what I have scheduled that day.				
3. Once a week or so, I look at my calendar and make a plan for the week.				
4. I keep a written list of things I need to do.				
5. I keep a written list of appointments I need to go to.				
6. I remember to do certain things by pairing them up with other things that I do on a regular basis (eg, remember to clean out the refrigerator every time I come home with groceries).				
7. I remember where things are by putting them in the same place all the time.				
8. If I need to remember something, I write it down somewhere.				
9. I place reminders for myself where I am sure to see them.				
10. I remember things by creating visual pictures in my mind.				
11. I take notes on things I want to learn and remember.				
12. If I want to remember something I’ve just heard, I repeat it to myself over and over.				
13. I remember things by linking new information to information I already know.				
14. I use acronyms to remember things.				
15. I put things I have to remember into categories.				
16. I use rhymes to remember things.				
17. If I want to learn something, I study it over and over until I know it by heart.				
18. I repeat back what I hear to make sure I’ve understood things people tell me.				
19. I make eye contact with someone who is talking to help me understand what is being said.				
20. To stay focused, I talk to myself while I’m working on a task.				

21. If I don't understand something that someone says, I ask the person questions about it until I am sure I understand.				
22. I usually stick to a daily schedule.				
23. My living space is organized so there is a place for everything, and everything is in its place.				
24. I use brainstorming to help me solve problems.				
25. I use a problem-solving method to help me solve problems.				
26. When I am solving a problem, I talk myself through it, step by step.				
27. I test out my ideas to see if they are accurate.				
28. I test out ideas by gathering "pro" and "con" evidence.				
29. When I am working on something, I monitor myself to see how I'm doing.				
30. When I'm having trouble solving a problem, I switch to a different strategy.				