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Cognitive Remediation and Vocational Rehabilitation for Schizophrenia

Bruce E. Wexler[1–3] and Morris D. Bell[3–5]

[2]34 Park Street, New Haven, CT 06519; [3]Yale University Department of Psychiatry; [4]Connecticut Mental Health Center; [5]Veteran Administration's Connecticut Health Center

Cognitive deficits are a central and debilitating aspect of schizophrenia and other major mental illnesses. Although they are largely refractory to pharmacotherapy, multiple studies have now shown that large and lasting improvements in cognition can result from behavioral interventions. We will review our work over the past 10 years demonstrating that cognitive remediation treatment together with work therapy or supported employment can lead to large, lasting, and clinically relevant improvements in cognition and work functioning. While we will make some references to the work of others in these same areas, this is not a general review of these areas of research. Instead, the goal is to provide the rationale for the progression of our studies, describe the methods, and summarize the results, so that readers may understand, critique, and improve upon what we have done.

Key words: schizophrenia/cognitive deficits/cognitive remediation/vocational rehabilitation

The Problem

Cognitive Dysfunctions in Schizophrenia

Most realms of cognitive, motor, and sensory function have been shown to be abnormal in patients with schizophrenia. Different reviewers of this extensive literature use somewhat different taxonomies to classify function, but abnormalities have been documented in attention, executive function, motor performance, spatial abilities, language, and memory;[1] concentration/speed, executive function, sensory/perception, language, spatial memory, and verbal memory;[2] and attention vigilance, abstraction flexibility, verbal intelligence and language function, spatial organization, verbal memory and learning, visual memory, speeded visual-motor processing and attention, and fine motor functions.[3] While essentially all aspects of cognition have been shown to be abnormal, studies suggest that some deficits may be more severe or more basic. Two careful studies using a broad assessment battery, moderately large patient samples, and analytic procedures to compensate in part for differences in difficulty among tests indicate that deficits may be particularly pronounced on tests of verbal memory and learning.[3–4] Some investigators have suggested that relatively specific deficits in a fundamental cognitive process such as working memory[5] or attention[6] may be of primary pathophysiologic significance and give rise to other performance deficits. Others suggest that there may be subgroups of patients currently diagnosed as having schizophrenia who differ in underlying pathology and in the nature of their cognitive deficits. In our laboratory, for example, we have identified a subgroup of patients with normal attention and normal or superior performance on nonverbal tests of working memory but marked deficits in verbal working memory.[7–9]

Cognitive Dysfunctions Are Associated With Measurable Abnormalities in Regional Brain Activation

Functional magnetic resonance and other available brain-imaging methods are sensitive enough to measure regional brain activation abnormalities associated with the observed cognitive deficits. Decreased activation of the frontal cortex in patients with schizophrenia during language generation, verbal memory, and other cognitive tasks has been found in multiple studies.[10–19] These frontal activation deficits may be part of a broader activation failure of a cortical-cerebellar-thalamic-cortical system, at least during verbal memory tasks.[20] Some studies report abnormal increases in parietal or temporal activation while at the same time finding deficits in prefrontal activation.[11, 14, 16] Other studies have reported abnormalities during tasks requiring sustained attention and simple sensory processing, with decreased activation of the left superior temporal gyrus but increased activation of the right middle temporal gyrus while subjects listen to speech,[21] increased visual cortex activation with photic stimulation,[22–23] and decreased activation of the right superior temporal gyrus[24] and the middle frontal and left anterior temporal cortex[25] during auditory target–detection tasks. Several studies have demonstrated

[1]To whom correspondence should be sent; tel: 203-974-7339, fax: 203-974-7881, e-mail: bruce.wexler@yale.edu.

decreased task-related activation of the anterior cingulate cortex in patients.[12, 20, 26–27]

Functional Significance of Cognitive Deficits

In multiple studies, cognitive dysfunctions have been strongly correlated with poor psychosocial function, with associations between psychosocial function and cognition often greater than associations between psychosocial function and clinical symptoms.[28–29] Several investigators have described neurocognitive deficits as "rate-limiting factors" in work capacity.[28, 30–31] Our research group found that cognitive impairment affects the rate of improvement on work performance measures in our work program[32–33] and that neuropsychological testing can predict 78% of the variance in individual improvement in work quality.[34] Moreover, we have identified a subgroup for whom these impairments are particularly severe. These subjects had more difficulty on the job, worked fewer hours and fewer weeks, and made fewer clinical gains than other patients in our work program. Cognitive deficits also discriminated subjects who completed the program from those who did not.[35] A recent review of the relationship between cognitive deficits and functional outcomes has emphasized the importance of developing new treatment for these deficits.[36]

Cognitive Remediation Treatment

Cognitive Enhancement Therapies

Beginning over 25 years ago a series of studies has suggested that cognitive deficits in patients with schizophrenia can be improved by a variety of training strategies.[37–40] Similar results, if somewhat less consistent, have been reported with treatment of individuals with traumatic brain injury.[41] There are 2 general approaches: compensatory strategies that enable someone to circumvent a defective cognitive processor and cognitive remediation training (CRT) exercises that enhance or restore the defective function.

Compensatory Strategies. Compensatory strategies for brain injuries can be as simple as providing notepads to help patients with memory loss[42–43] or as painstaking as rebuilding speech using intact, formerly nonlinguistic lip and mouth movements such as spitting, blowing, and kissing.[44] In patients with schizophrenia, repeated studies have demonstrated that providing detailed instructions can lead to significant improvement on the Wisconsin Card Sorting Test (WCST).[45–51] In several studies monetary reinforcement enhanced outcome. These results are particularly impressive since poor performance on the WCST[52] is associated with executive function deficits in schizophrenia and with prefrontal activation deficits in brain-imaging studies (e.g., [53]). Successful compensatory instruction has also been reported for the Tower of Toronto Puzzle,[54] the Span of Apprehension Test,[55] and tests of sustained attention,[56] although not all efforts have proved effective (e.g., [57]). Recent work has extended this approach to teaching patients compensatory or adaptive skills to deal with the effects of cognitive deficits in their personal real-world environments.[58] Patients receiving this cognitive adaptation training had decreased positive and negative symptoms, increased motivation, and higher levels of global functioning relative to control groups.

Restorative Strategies. The exciting possibility of restoring lost elemental brain function through cognitive retraining has gained support from studies of brain plasticity in adult, nonhuman primates. These studies have demonstrated conclusively that extensive repetition of the same activity leads to an increase in the number of cortical brain cells active during that particular task (reviewed in [59]). For example, if adult monkeys perform a fine motor task requiring the manipulation of very small objects with their fingers 1,000 times, areas of the brain representing somatosensation from task-relevant areas on the fingertips grow to include many new neurons.[60] Potential for "disuse atrophy" of associated neural resources is also suggested by these results.[61] Cognitive dysfunction in schizophrenia could be compounded by such a process, as activities that involve areas of deficits are avoided and unrewarded. Therapeutic exercise or practice of these functions and activation of the associated neural centers could, at least, reverse such atrophy and, at best, decrease the initial deficit.

In an initial test of this possibility, we had 22 clinically stable, medicated outpatients with schizophrenia participate in 4 or 5 training sessions per week for 10 weeks. Half of the patients practiced a visual reading task, and half, a spatial memory task. All practiced a unimanual motor speed and dexterity task. In order to engage the target neurocognitive systems and provide a sense of success and accomplishment, tasks were initially made easy enough for patients to do them successfully. Over the 10 weeks of training, stimulus duration and the interstimuli response interval were gradually shortened, and overall task duration was gradually lengthened. The rate of changes was determined for each patient individually, with the dual goals of continually challenging each patient and still maintaining performance accuracy at 85–95%. Performance-based monetary rewards were given to enhance motivation and the personal sense of accomplishment. Healthy and successfully employed individuals were tested on the training tasks in order to determine whether patients were able to achieve normal performance levels after training. The healthy subjects practiced the task long enough to become familiar and comfortable with the procedures and were

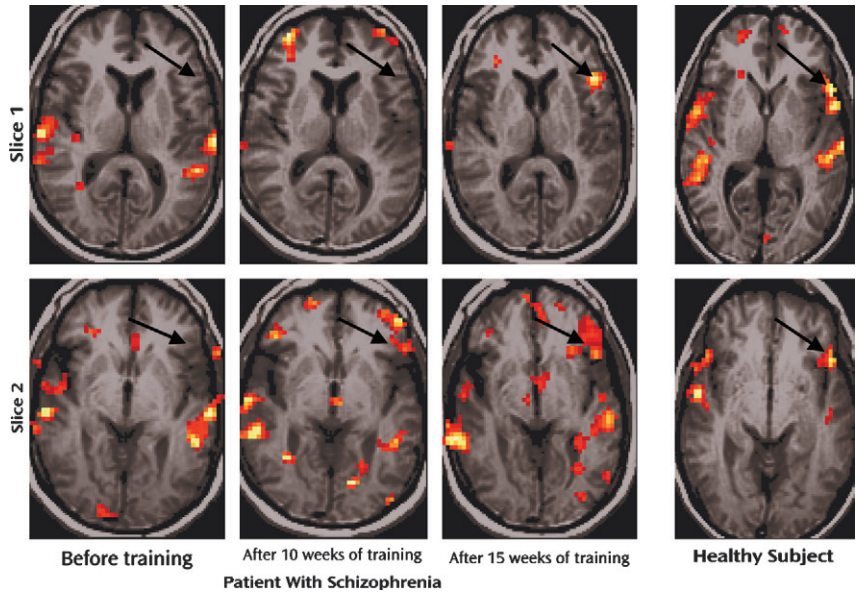

Fig. 1. Left Inferior Frontal Regional Brain Activation in a Patient During a Verbal Working Memory Task Before and After Cognitive Remediation Training and in a Typical Healthy Individual.

then tested with task difficulty levels similar to those reached by the patients at the end of training. After 10 weeks of exercises, 16 of the 22 patients performed as well as or better than the best healthy subject on the verbal reading and spatial memory tasks. For example, by the end of training on the verbal task, 6 of the 11 patients were doing the task with stimulus exposures less than or equal to 100 milliseconds, with their performance accuracies ranging from 93 to 99%.

This initial study demonstrates that on 2 tasks with which patients with schizophrenia have repeatedly been found to have significant difficulty (sustained and rapid language processing and spatial memory), repeated practice with incremental adjustments of difficulty led to normal or even supernormal performance. Apparently the necessary neural substrates are not missing or destroyed.

Neuroimaging Confirmation of Changes in Cognition-Related Brain Activation

In order to see if cognitive exercises enhance task-related brain activation, we used functional magnetic resonance imaging to study 8 patients before and after 10–15 weeks of verbal memory exercises.[62] The exercises were 2 different auditory serial position tasks in which short lists of 2 to 6 words were presented, and after delays of 1–14 seconds, 1 of the words was repeated. Subjects had to indicate where the repeated word was in the original sequence (i.e., first, second, third, etc.). In 1 task, different words were used on each trial. In the other, more difficult task, the same words were used on all trials. We had previously shown that patients with schizophrenia do more poorly than healthy subjects on these tasks[63] and show lower than normal activation of the left inferior frontal cortex while doing the tasks.[17]

One patient who showed particularly robust performance improvements after the 10-week training period was given 5 additional weeks of training, beginning 6 weeks after the initial 10-week training ended. After the combined 15 weeks of training, this patient showed a 50% performance increase in a series of practiced and unpracticed auditory and visual verbal serial position tasks. The changes in brain activation while doing the auditory serial position task (4-word lists) over the course of training are shown in figure 1. The fourth column shows data from a typical healthy control; note the strong temporal and left inferior frontal activations. Prior to treatment, this patient showed relatively normal temporal activation but essentially absent left inferior frontal activation. There is evidence of left inferior frontal activation in this patient after 10 weeks of cognitive training, and after 15 weeks of training the activation of this area appears similar to that seen in healthy subjects. In the overall sample of patients, the degree of functional improvement on the memory tasks was significantly correlated with the percent of increase in left inferior frontal activation ($r = .66$, $p < .04$).

Review Articles and Other Research Support for Cognitive Remediation

Several reviews of cognitive remediation have now been published.[51, 64–68] All but the Pilling et al. review[66] conclude that the literature favors clinical benefit of 1 type or another. Twamley et al.[68] provide the most comprehensive and up-to-date review of randomized clinical

trials and offer several important observations about cognitive remediation as a scientific endeavor. Importantly, they note the awkwardness in a newly emerging field of having no consensus on terms. They point out that cognitive training may refer to cognitive remediation, which implies a curative or restorative treatment (our approach), compensatory training, or environmental approaches, which manipulate the environment to decrease cognitive demands. Even among those studies using cognitive remediation there are important differences in method between those using computer-assisted methods, which practice progressively more difficult and complex cognitive functions,[69–71] and metacognition training (e.g., [72–73]), which employs strategy-oriented task practice. Moreover, while most intervention trials employed cognitive training on its own, 2 studies, ours[69] and Spaulding et al.,[74] used cognitive training as part of a comprehensive rehabilitation program. Twamley et al. have found 17 randomized clinical trials in the literature and calculated weighted mean effect sizes (Cohen's *d*): for improvements in neuropsychological performance = .32, for reductions in symptom severity = .26, and for improvements in everyday function = .51.[68] However, only 3 studies examined functional outcomes, and the 1 study involving environmental manipulation contributed the most to the effect size.[58] These reviews reveal that very little evidence exists for cognitive remediation effects beyond such proximal outcomes as improvement on trained tasks or on closely related but untrained neuropsychological tests. In the next section we will describe our current studies and how they support efficacy for more distal outcomes, especially for improved work functioning.

Combination of Cognitive Remediation and Vocational Rehabilitation

We have conducted 2 studies to evaluate the effects of adding CRT to vocational programs. We reason that the cognitive exercises might make it possible for patients to gain more from the vocational interventions and that work activity could provide opportunities for patients to practice and generalize cognitive gains made in the laboratory. The first study using work therapy (WT) was begun in 1998 and ended in 2003.[35, 69] The active treatment was for 6 months, with follow-up at 1 year. The second study using a community-based supported employment (SE) program was begun in 2001 and is ongoing. The active treatment was for 12 months, with follow-up at 2 years.

Both studies recruited outpatients with schizophrenia or schizoaffective disorder as determined by Structured Clinical Interviews for DSM-IV, who were in a post-acute phase of illness. Patients with developmental disabilities, neurological disease, substance abuse within the past 30 days, or Global Assessment of Functioning scores below 30 were excluded. The WT study included 145 patients, while the SE study has recruited 77 subjects thus far. Both samples have severe and persistent illness (average of 10 hospitalizations over 15 years of illness with current Positive and Negative Syndrome Scales scores in the 70s), although the SE sample has an earlier age of first hospitalization (21 versus 25 years) and is somewhat younger (38 versus 41 years), with a somewhat lower IQ (84 versus 87). Both samples are similar in their psychopharmacological treatment, with most (80%) being treated with an atypical antipsychotic at moderately high doses (average 740 chlorpromazine equivalents). The most important difference between samples is gender, with 22% female in the WT sample, which was drawn primarily from a Veterans Administration hospital population, and 45% female in the SE sample, which was drawn primarily from a community mental health center.

Subjects in both studies were randomized into work services plus CRT (CRT + WT or CRT + SE) or work services (WT or SE) alone. Randomization is stratified by work experience (1 year of continuous full-time employment at the same job) or severe cognitive impairment (1 SD below a schizophrenia sample's performance on at least 2 of 6 neuropsychological tasks),[35] and resulted in no significant differences in background characteristics between conditions.

CRT consisted primarily of computerized exercises of attention, memory, language operations, and problem solving 3–6 hours/week. In the WT study, patients in CRT also did a selective attention listening task for approximately 1 hour/week and participated in 2 weekly discussion groups. One focused on cognitive and work performance and included specific work feedback;[75] the other focused on social information processing (SIP). The WT-only group had the weekly work feedback group. Patients were paid $3.40/hour for work or participation in CRT up to a maximum of 20 hours/week with bonus pay up to $8.40/hour for doing 5 hours/week of CRT or 15–20 hours of work, worked at the VA Medical Center, and were eligible to continue work after completion of the 6-month study treatments. They might continue in their work therapy job, be accepted into a competitive-wage job through another VA program, or seek their own job in the community.

The main differences in methods between the WT study and the SE study were the provision of a hybrid SE program[76] that found regular jobs in the community, use of transitional funds to pay patients during the initial months of work in community jobs and thereby overcome barriers that prevent them from being given the opportunity to work, greater emphasis on exercise of language-related cognitive operations, extension of CRT to 1 year, provision of daily performance-based rewards in addition to hourly pay for CRT, and a competitive wage ($7.10/hour) for both CRT and work. As in the WT study, patients in the SE + CRT

Table 1. Cognitive Training Tasks

Training Tasks	Component Cognitive Processes						
	Simple Attention	Switch Attention	Response Inhibition	Memory	Language Mediation	Category Formation	Planning/ Strategy
Simple Attention							
Letters	xx		x		x		
Words	xx		x		xx		
Color–Shape	xx		x				
Simple Auditory	xx						
Simple Visual	xx						
Random Small	xx						
Complex Attention and Response Inhibition							
Simple Choice							
Auditory	xx		x				
Random Small	xx		x				
Simultaneous Multiple Attention	xxx	xxx	xx				xxx
Alternating Attention	xx		xxxx				
Memory							
Sequential Recall							
Digits Auditory	x			xxx	xx		
Digits Visual	x			xxx			
Reverse Digits Auditory	x			xxx	xx		
Reverse Digits Visual	x			xxx			
Words Visual	x			xxx	xx		
Graphics Visual	x			xxx	x		
Language							
Synonyms	xx				xxx		
Antonyms	xx				xxx		
Text–Picture	xx				xxx		
Phonetics	xx				xx		
Rhymes	xx				xx		
Category Formation							
Verbal Memory Categorizing	x			xx		xxx	
Exemplars	xx		x		xx	xxx	
Planning and Strategy							
Knights Challenge	x		x				xxxx

Note.—The number of x's indicate importance of component cognitive processes in each training task.

group participated in the cognitive and work performance feedback group and the SIP group. The SE-only patients participated in the workers support group as in the WT study but also participated in a group that focused on lifestyle changes.

Selected Targets for Cognitive Training Exercises

For these studies we created a multidimensional CRT with a series of exercises and standardized criteria for moving patients from 1 exercise to the next. We used 3 well-established facts about cognitive dysfunction in schizophrenia to guide us in selecting exercises for the CRT: (1) groups of patients on average show abnormalities in nearly all aspects of cognition and on nearly all tests of cognition; (2) there is some evidence and/or theoretical suggestion that deficits in attention, working memory, and/or language-mediated cognitive operations may be particularly severe and may underlie deficits on other tests; and (3) the degree and nature of deficits vary widely from person to person. The first fact led us to include exercises of a wide range of cognitive operations in our battery. The second fact led us to emphasize exercises of attention, working memory, and language-related cognitive operations. Given the suggestion that at least in some patients disorders of attention compromise more complex cognitive operations (e.g., [7]), we have followed the lead of Brenner et al.[77] and focused on training attention in the first exercises offered and moving

patients on to exercises of other functions after extensive attention training. The specific tasks and the cognitive functions they exercise are listed in table 1.

We considered 2 approaches to the problem of marked interindividual variation in the patterns of cognitive strengths and weaknesses. One was to customize the interventions based on initial assessments of each patient's strengths and weaknesses. The usefulness of this approach, however, would depend upon the accuracy, clarity, and reproducibility of the assessment. It would also require expertise in the administration and interpretation of a range of assessment tests. As a result of these concerns, we chose instead to allow the CRT to shape itself to each patient's strengths and weakness by moving patients quickly through exercises with which they had little or no difficulty and focusing their treatment time on their individual areas of cognitive deficit. In brief, each task in the CRT has progressive difficulty levels, as well as specified performance criteria necessary to move from 1 level to the next and to eventually graduate from the task. Through these incremental increases in task difficulty, the CRT not only can determine simply whether an individual does or does not need treatment in a particular area but also can find the level within each task where an individual experiences difficulty. The repeated presentations of the task at progressive difficulty levels even for people who do well at it allows repeated confirmations that performance is intact in that area before moving on to other areas. When a patient does poorly on a task the program keeps him or her on the task for intensive training.

We initially set tasks at very easy levels, continuously monitored patient performance, and increased or decreased task difficulty to maintain performance at the right balance between success and challenge. Using the performance levels of laboratory personnel and the performance levels attained by the initial groups of patients after training as a guide, we established graduation criteria for each exercise. When patients met graduation criteria for a particular task they moved on to the next task in the training sequence. Some patients proved unable to reach the graduation criteria on a given task even with repeated practice. Review of the patterns of improvement indicated that patients who showed the same performance level on a task for 8 successive training sessions seldom, if ever, showed performance gains with more practice. To prevent patients from becoming stuck on such tasks, we moved them on to the next task.

Generalization of Cognitive Gains to Tasks Not Practiced in the Computerized Exercises

In the WT study, we compared changes in neuropsychological test performance from baseline to 6-month follow-up (end of the active intervention) for subjects in CRT + WT with those for subjects in WT.[69] To reduce experiment-wise error, 21 neuropsychological variables were subjected to factor analysis to produce 4 groupings of variables: executive function, working memory, thought disorder, and visual and verbal recall. These groupings were used as dependent variables in multivariate analyses of covariance of follow-up scores, with intake scores as covariates. Patients receiving CRT + WT showed greater improvements on executive function ($p < .006$) and working memory clusters ($p < .01$). The thought disorder and visual and verbal recall factors had nonsignificant trends favoring CRT + WT. Significant individual variables included Wisconsin Card Sorting Test Conceptual Level ($p < .002$), WCST Categories Correct ($p < .04$), WCST Nonperseverative Errors ($p < .004$), Bell Lysaker Emotion Recognition Test (BLERT;[78] $p < .001$), and Digit Span Backward (Wechster Adult Intelligence Scale III [WAIS-III];[79] $p < .05$). For many patients the functional gains were substantial, with improvements greater than 0.8 SD in 35% of patients on the WCST Conceptual Level, 39% on Digits Backward, and 39% on the BLERT.

For the current SE study we have done a preliminary analysis based on 54 subjects who have completed 12-month follow-up.[80] Using the same factor groupings and analysis as the WT study, the CRT + SE condition showed significantly greater improvement than the SE-only condition on executive function ($p < .05$), with WCST Categories Complete ($p < .03$), WCST Conceptual Level ($p < .05$), and Trials to First Category ($p < .05$) being individually significant. The other factors failed to reach significance, although all had trends in the direction favoring CRT + SE, with Digit Span ($p < .05$) and Arithmetic (WAIS-III;[79] $p < .01$) being individually significant. Moreover, CRT + SE also showed significantly greater improvement ($p < .05$) on the cognitive component[81] of the Positive and Negative Syndrome Scale,[82] indicating that observable features of cognitive impairment (such as conceptual disorganization, stereotyped thinking, and poor attention) had improved.

Normalization of Neuropsychological Test Performance

A stringent test for the clinical significance of an intervention is whether it can return patients to normal levels of function.[83] We define normal functioning as a standardized score of 90 or greater on WCST, as a BLERT threshold based on 15 (of 21) correct or better, and for Digits Backward as performing within 2 digits of the subject's own Digits Forward (WAIS-III)[79] score (for full details of the criteria for normal functioning and type of analysis, see [69]). The WT sample has been analyzed with these criteria, and the percentage of CRT + WT subjects with normal scores on the BLERT increased from 35 to 60%, whereas the percentage of WT patients with normal scores declined from 47 to 42% ($p < .05$). For Digits Backward, the proportion of CRT + WT subjects increased from 45

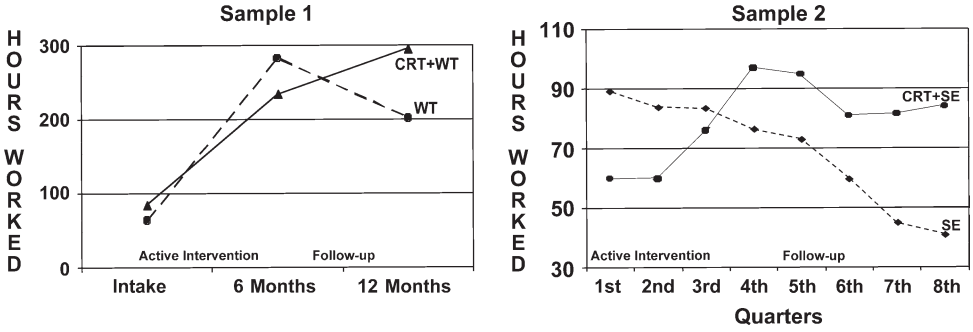

Fig. 2a–b. Hours Worked by Condition During 26-Week (Work Therapy Study) or 52-Week (Supported Employment Study) Time Period.

to 77%, while WT patients decreased from 56 to 45% ($p <$ .01). These findings provide evidence not only that patients as a group show statistically significant group mean improvements in cognitive functioning following CRT + WT but also that many actually reach performance levels similar to those of healthy subjects.

Durability of Training Effects

At 12-month follow-up of the WT study, 6 months after the completion of training for everyone (although some had stopped training much earlier), the proportion of subjects in CRT + WT with normal performance on a digits recall task was sustained and was significantly greater at follow-up than for subjects in WT.[84] Neuropsychological testing at 12-month follow-up also demonstrated the durability of training effects. Repeated measures analysis of variance revealed that subjects receiving CRT + WT showed significantly greater improvements on executive function ($p < .05$) and working memory ($p < .01$) clusters than the WT group. As many as 60% showed sustained improvement on some measures. A comparison of effect sizes over time shows the durability of training effects. Analyses of individual measures over time by condition indicate significant linear trends for Digits Backward ($p < .01$), Trails B[85] time ($p < .05$), WCST Categories Complete ($p < .01$), and WCST Conceptual Level ($p < .01$). Sometimes improvement continued during the 6-month period following the active intervention. This phenomenon of continued benefit may suggest that the intervention sets in motion improvements that build on their own success or that it takes time for a consolidation of cognitive gains to be fully realized.

Improvement in Cognitive Performance on the Job

In order to evaluate the role of cognitive function on the job as a possible mediating variable between laboratory gains in cognition and job success, our group developed the Vocational Cognitive Rating Scale (VCRS)[80] administered by job coaches who directly observe and interact with the patients around work tasks. Preliminary analyses in our current SE study show significantly greater improvements (comparison of the average of the last 3 VCRS scores with the average of the first 2 VCRS scores covaried out using analysis of covariance [ANCOVA]) for CRT + SE versus SE on VCRS total score, VCRS Memory subscale, and VCRS Attention subscale ($p <$ .05). These findings provide an important link between the neuropsychological and functional magnetic resonance imaging results (see below) and functional change on the job. They indicate that patients' cognitive ability on the job was sufficiently altered by CRT + SE that job coaches could observe and record these improvements.

Improvement in Work Performance

To evaluate the effects of CRT on work performance we compared the final 3 biweekly ratings on the Work Behavior Inventory (WBI)[86–87] for CRT + SE patients to the same ratings for SE-only patients, with the average of the first 2 WBI ratings at study entry as a covariate in ANCOVA. The average of the initial 2 scores provides a more stable baseline than the first score alone and yet does not extend too far into the treatment period. Use of the final 3 scores again increases score stability and minimizes the effects of "end of study" anxiety that might be evident in the final assessment alone. CRT + SE patients showed significantly greater improvements on WBI total score ($p < .05$) and WBI Social Skills ($p < .05$), Personal Presentation ($p < .05$), and Cooperativeness ($p < .05$). WBI Work Habits and Work Quality showed nonsignificant trends favoring CRT + SE. These findings suggest that CRT may be increasing the capacity of patients to function on the job and benefit from the work experience. The benefits seem to include social and interpersonal function, which are often crucial for sustaining employment.

Durability of Employment Gains

To determine the durability of employment gains related to CRT, we used repeated measures analyses to compare conditions on total hours worked and on the percentage of patients employed. Employment data were collected

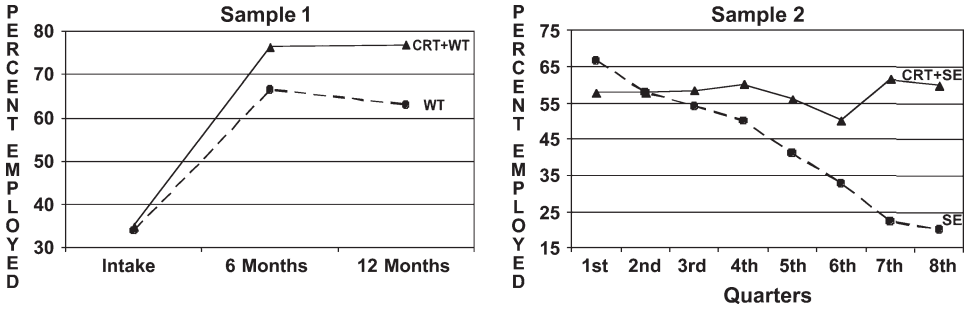

Fig. 3a–b. Percentage Employed by Condition at Specified Time Points Throughout the Study and Follow-up.

6 months after the end of the 6-month WT program (N = 145) and 12 months after the cessation of the 12-month SE program in the patients who had thus far completed the 2-year follow-up in the SE study (N = 43). For hours worked, the time by condition interaction was significant in both studies. The patients receiving CRT maintained or increased the number of hours they worked during the follow-up period, while hours worked decreased in the other conditions ($p < .05$ for WT study [figure 2, sample 1]; $p < .05$ for SE study [figure 2, sample 2]). Results are similar when the percentages of patients employed are considered (figure 3). Employment rates are much higher in the WT study because of placement in noncompetitive jobs in the medical center rather than community employment. There is still a suggestion that CRT + WT patients were more likely to remain employed after the end of treatment than WT-only patients. With the greater demands of competitive community employment and longer post-treatment follow-up in the SE study, this difference is marked and significant. Twelve months after the end of treatment, 57.5% of patients in the WT + CRT group were still employed, while this was true for only 21.0% of patients in the WT-only group (chi-square 7.1, df = 1, p = .01).

More Evidence Linking CRT With Employment Gains

Two analyses provide further evidence that CRT is associated with employment gains. First, in the WT study, we identified subjects as responders to CRT by virtue of them having increased performance from below normal to normal (within 1 SD of the performance of healthy subjects) on digits recall by the conclusion of training. During the 6 months after treatment ended, these subjects worked on average 390 hours. In contrast, subjects in the WT condition who also had normal digits recall at follow-up worked only 130 hours during the 6 months post-treatment (intergroup difference $p < .0001$). Thus, being able to recall digits normally was not what made the difference; rather, being a responder to the CRT training was key.

Second, in the SE study, we looked at the relationship between a composite score of performance on the job at the end of year 1 and hours worked during year 2. The relationship was stronger for subjects receiving CRT, with R^2 = .36 ($p < .001$) in the SE-only condition and .60 ($p < .0001$) in the CRT + SE condition. We hypothesize that CRT helped subjects to optimize the benefits of their rehabilitation experience so that their achievements in the first year had more of an effect on their vocational outcomes during the second year. When the full study sample is available, we will evaluate models that more thoroughly examine the relationships among possible mediator variables and eventual year 2 outcomes.

Conclusion

Cognitive deficits are an incapacitating aspect of schizophrenia and other major mental illnesses that are largely refractory to currently available medications. Basic neuroscience research has shown that unusually intense and extended activation of neuroprocessing systems causes those systems to recruit neural resources that could enhance their functioning. Disease-related impairment of a cognitive system can lead to both underfunctioning and underuse of the system and a worsening cycle of disuse atrophy. Our work and that of others suggests that intensive activation of underfunctioning cognitive systems in patients with schizophrenia can lead to enhanced function of the system, greater task-related activation of the relevant brain areas, and generalized and lasting improvements in cognition. Moreover, these benefits may translate to greater success in the workplace. More work is needed to increase the effects of these new interventions and to test their impact on functional outcomes.

Acknowledgments

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