



Predictors of change in life skills in schizophrenia after cognitive remediation

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ABSTRACT

Few studies have investigated predictors of response to cognitive remediation interventions in patients with schizophrenia. Predictor studies to date have selected treatment outcome measures that were either part of the remediation intervention itself or closely linked to the intervention with few studies investigating factors that predict generalization to measures of everyday life-skills as an index of treatment-related improvement. In the current study we investigated the relationship between four measures of neurocognitive function, crystallized verbal ability, auditory sustained attention and working memory, verbal learning and memory, and problem-solving, two measures of symptoms, total positive and negative symptoms, and the process variables of treatment intensity and duration, to change on a performance-based measure of everyday life-skills after a year of computer-assisted cognitive remediation offered as part of intensive outpatient rehabilitation treatment. Thirty-six patients with schizophrenia or schizoaffective disorder were studied. Results of a linear regression model revealed that auditory attention and working memory predicted a significant amount of the variance in change in performance-based measures of everyday life skills after cognitive remediation, even when variance for all other neurocognitive variables in the model was controlled. Stepwise regression revealed that auditory attention and working memory predicted change in everyday life-skills across the trial even when baseline life-skill scores, symptoms and treatment process variables were controlled. These findings emphasize the importance of sustained auditory attention and working memory for benefiting from extended programs of cognitive remediation.

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1. Introduction

Over the past twenty years, incontrovertible evidence has shown that individuals diagnosed with schizophrenia show 1–2 standard deviation impairments on a variety of measures of neurocognitive function, including attention, episodic and working memory, language, and problem-solving relative to healthy, demographically matched controls (see Reichenberg and Harvey, 2007; Heinrichs and Zakzanis, 1998 for reviews).

These deficits are present at disease onset (e.g., Saykin et al., 1994), stable over time (e.g., Gold et al., 1999; Hoff et al., 1999; Kurtz et al., 2005; Stirling et al., 2003), and are only modestly affected by pharmacologic intervention for symptoms (e.g., Keefe et al., 2007).

Particular significance has been attached to these deficits, as there are a growing number of studies showing that deficits in elementary neurocognitive function are linked to a variety of aspects of functional outcome and thus may contribute substantially to the profound social disability that frequently accompanies the disorder (e.g., Salkever et al., 2007). Reviews suggest that neurocognitive deficits explain 20–60% of the variance in studies of the ability to solve interpersonal problems, community (social and occupational) function

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and measures of skill acquisition in rehabilitation programs (see Green et al., 2000, 2004 for reviews). Many of these studies also suggest that neurocognitive deficits are more closely linked to functional outcome than are psychiatric symptoms (e.g., Green et al., 2000). These results lend support to the contention that treatment targeted at attenuation of these deficits will produce improvements in related community function.

Over the past 10–15 years a rapidly growing number of randomized controlled studies have investigated the efficacy of a group of behavioral interventions, collectively labeled cognitive rehabilitation, that are focused on improving neurocognitive function in persons with schizophrenia directly through repeated task practice and/or providing behavioral strategies to circumvent these deficits. Initial studies have yielded promising findings (e.g., Bell et al., 2001; Medalia et al., 2001), and meta-analyses of the extant literature have confirmed medium mean effect-sizes for this group of interventions ($d = .41$) when cognitive task performance is selected as an outcome measure (McGurk et al., 2007).

Judgments regarding the ultimate value of cognitive rehabilitation as a treatment strategy, however, will lie in its potential impact on outcome measures that represent a generalization of training effects to more molar measures of life function. While very small in number, initial studies of the ability of the effects of cognitive remediation to generalize to a variety of aspects of real-world functioning have been positive (e.g., McGurk et al., 2005), with meta-analyses revealing significant mean effect-sizes ($d = .35$), only slightly lower than those reported for cognitive outcome measures (McGurk et al., 2007).

Despite these positive group findings, results to date reveal substantial individual differences in response to cognitive remediation interventions. A recent summary of three cognitive remediation trials found improvement rates for a mixed group of psychiatric patients that ranged between 40 and 69% for individuals (Medalia and Richardson, 2005). Thus, determining the treatment process, neurocognitive or symptom factors that may predict a strong response to cognitive remediation will be crucial for matching patients to appropriate treatment and modifying extant treatments to treat individuals not currently benefiting from these treatments.

Only two studies, to our knowledge, have investigated baseline predictors of response to cognitive remediation interventions. Fiszdon et al. (2005), studied 58 patients with schizophrenia and evaluated the relationship of demographic, symptom, process and neurocognitive variables to the probability of showing normalized performance (improvement to within 1 SD of healthy control performance) after training on a memory task that served as an element of a comprehensive, computer-assisted remediation program. The authors' hypothesized that stronger sustained vigilance at study entry would predict a greater likelihood of normalized performance after the remediation intervention. As predicted, results revealed that sustained visual vigilance, along with immediate verbal memory, time between termination of intervention and follow-up assessment, and measures of hostility accounted for 70% of the variance in chances of normalization on the selected memory task in this cognitive remediation protocol.

Medalia and Richardson (2005) have reported that motivation, as indexed by voluntary participation in cognitive remediation sessions (treatment intensity), along with work style, and clinician experience were most closely linked to a positive response to cognitive remediation treatment. Neurocognitive measures of sustained attention, but not processing speed, working memory and immediate story recall were also related to improvement across several mixed samples of psychiatric in and outpatients. Improvement in the study was measured by standardized neurocognitive measures distinct from the Neuropsychological and Educational Approach to Remediation (NEAR) treatment program employed in the study. Patients were classified as "improved" if they improved on any measure of neurocognitive function to a degree that could have occurred by chance only 5 times or less out of 100.

One study evaluated the mediating effect of cognitive remediation on the relationship of change in neurocognition and associated change in psychosocial function over a three-month treatment trial. Reeder et al. (2006), in an investigation with 85 patients with schizophrenia and impaired executive function/memory, showed that improvements in executive functioning were accompanied by improvements in clinician-rated psychosocial status across experimental and control groups.

Taken together, these findings suggest that treatment intensity, along with sustained attention, predicts response to remediation interventions when outcome is indexed as either an improvement on tasks trained in the remediation protocol, or neuropsychological measures distinct from those trained in remediation and that change in executive-function across time in cognitive remediation treatment trials may be linked to change in clinician-rated psychosocial function. No study, to our knowledge, has focused on pre-treatment predictors of generalization of improvement from cognitive remediation interventions to measures of capacity-based everyday functioning in a diagnostically homogenous group of patients with schizophrenia. The goal of the current study then was to evaluate the relationship of neurocognitive, treatment, and symptom variables to improvement on a measure of functional capacity across an extended period of cognitive remediation treatment. We predicted that baseline neurocognitive status and treatment intensity, but not symptoms, would predict change in functional capacity across the treatment trial.

2. Methods

All study procedures met with institutional ethical approval. Patients who agreed to take part in the study gave written, informed consent at the time of their entry to outpatient rehabilitation and were randomly assigned to one of two computerized cognitive rehabilitation groups (cognitive remediation or computer-skills training). The results comparing the relative effects of these interventions on neuropsychological test performance in 19 of the cognitive remediation-treated participants described in this paper were previously reported (Kurtz et al., 2007). With the collection of data from 17 additional participants since the Kurtz et al. (2007) study, in the present paper we describe results from only those individuals randomly assigned to the cognitive remediation treatment condition of the parent study. A subset

of the current results was also described as a part of a study of improvement in functional capacity as a function of intensive rehabilitation treatment (Kurtz et al., 2008).

Cognitive remediation procedures were identical to those described previously (Kurtz et al., 2007) and consisted of an extended (100 h target) program of computer-assisted, drill-and-practice exercises carefully titrated for task difficulty and organized hierarchically. Sessions were administered three times per week for 30–45 min each and consisted of targeted training on sustained visual and auditory attention, response inhibition, shifting attention, working memory, semantic processing and verbal recall, as well as speeded language processing. Cognitive remediation was provided in addition to other day-program rehabilitation activities.

2.1. Participants

Thirty-six outpatients meeting DSM-IV (APA, 1994) criteria for schizophrenia or schizoaffective disorder as determined by the Structured Clinical Interview for DSM-IV (First et al., 1995) participated. Exclusion criteria for patients included auditory or visual impairment, evidence of mental retardation as indicated by a history of services evident from the medical record or a Vocabulary age-scaled score from the Wechsler Adult Intelligence Scale-III (WAIS-III) of less than 4, traumatic brain injury with a sustained loss of consciousness, presence or history of any neurologic illness, lack of proficiency in English, and/or criteria met for concurrent substance abuse or dependence. Recruitment for the study was continuous, over a period of seven years (2001–2008) and occurred at three sites. The majority of patients in the study ($n=31$) were recruited from and enrolled in an intensive outpatient program for patients with schizophrenia at The Institute of Living, Hartford Hospital's Mental Health Network (IOL) in Hartford, CT while other participants were recruited from social clubs at community mental health centers in Meriden, CT ($n=4$) and East Hartford, CT ($n=1$). Clients were assessed at the termination of the computer interventions, a mean 11.5 months (SD: 5.0) after study entry. Patients treated at The IOL were enrolled in a three-day per week program including structured group therapy, life-skills training, and exercise, whereas clients at the other two community mental health sites typically attended social clubs on a daily basis, but participated in a more limited set of group activities (e.g., daily food preparation). Demographic and clinical characteristics of the sample are presented in Table 1.

Table 1

Mean demographic and clinical characteristics of schizophrenia patients ($n=36$)

| Variable | Mean (SD) | Range |
|--|-------------|--------|
| Age | 32.4 (11.2) | 19–59 |
| Percent male | 69 | |
| Education | 13.4 (1.9) | 9–18 |
| Duration of illness (years) | 8.7 (8.7) | 1–31 |
| Age of onset (years) | 24.2 (7.3) | 13–42 |
| Number of hospitalizations | 3.9 (3.4) | 1–20 |
| Vocabulary Scaled Score (WAIS-III) | 10.8 (3.6) | 4–18 |
| Number of training hours | 52.6 (28.1) | 15–116 |
| Percent treated with atypical antipsychotic medication | 97% | |

Note: WAIS-III = Wechsler Adult Intelligence Scale.

2.2. Neurocognitive measures

Patients were assessed before and after cognitive remediation on a neuropsychological test battery. As the current study focused on predictors of treatment response, performance on neurocognitive measures at baseline was selected for all analyses. To reduce elevation of Type I error in the current study, measures of crystallized verbal intelligence, sustained auditory attention and working memory, verbal learning and memory, and problem-solving were selected from the larger battery. Measures of neurocognitive function were chosen based on their relationships reported in the literature to either cognitive remediation specifically, or psychosocial rehabilitation more generally. Sustained attention and verbal learning and memory measures were selected in light of their reported relationship to progress on specific elements of neurocognitive training in previous studies (Fiszdon et al., 2005; Medalia and Richardson, 2005) as well as skills training programs more generally (Smith et al., 2002), while problem-solving was selected in light of its observed relationship to outcome following supported employment rehabilitation interventions (McGurk et al., 2003). Neurocognitive testing and scoring was supervised by a doctoral-level psychologist. Measures of crystallized verbal IQ were included to ensure that links between specific neurocognitive functions and improvement in daily living skills after cognitive remediation could not be attributed to more global indices of verbal IQ.

2.2.1. The Vocabulary subtest from the WAIS-III (Wechsler, 1997)

An oral measure of word knowledge was used as an estimate of crystallized verbal ability. Age-scaled scores were selected as the independent measure.

2.2.2. Digit Span (WAIS-III; Wechsler, 1997)

A measure of sustained auditory attention and immediate verbal memory in which participants are asked to repeat serially presented numbers either forwards or backwards. Age-scaled scores were calculated as the independent variable.

2.2.3. California Verbal Learning Test-II (CVLT-II; Delis et al., 2000)

This is a list learning task in which 16 words from 4 semantic categories are read to the subject over a series of 5 list presentations. This test measures verbal learning, verbal memory and semantic organization. The learning slope across 5 trials was selected as the dependent measure as it reflects the average number of new words per trial that an examinee is able to recall, and thus provides a direct index of the ability of the participant to benefit from repetition of verbal information. Age-corrected z-scores for slope were selected as an independent variable. Long-delay free recall age-corrected z-scores were also selected to assess verbal episodic memory.

2.2.4. Penn Conditional Exclusion Test (PCET; Kurtz et al., 2004a,b)

The PCET is a measure of problem-solving. Results from several studies have shown evidence of construct validity in samples of healthy people (Kurtz et al., 2004a) and patients with schizophrenia (Kurtz et al., 2004b) for this task. The PCET requires the participant to select out one of four items based on one of three sorting principles. Participants must infer the sorting rule based on feedback to their responses. When the participant gets 10 consecutive correct responses, the sorting

principle shifts and there are a total of three sorting principles. Z-scores for errors computed from local normative data were selected as an independent measure.

2.3. Symptom measures

The Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) was used to assess symptoms at entry to the study and after the intervention. To understand predictors of treatment response, pre-intervention scores were used for all analyses in the current report. The PANSS is a semi-structured interview that generates ratings of signs and symptoms on 30 7-point Likert scale items. Symptom raters for the study maintained inter-rater reliability through periodic rater training sessions, and all raters were trained to a criterion reliability of .8 intraclass correlation coefficient (ICC), across four jointly viewed, but independently rated interviews. The subscales for total positive and total negative symptoms were selected as dependent measures.

2.4. Process variables

We measured treatment intensity by average number of hours of cognitive remediation completed per month and treatment duration by total hours completed across the intervention. With respect to treatment intensity, 34% of the sample received less than 4 h per month of cognitive remediation, 46% of the sample received between 4 and 6 h of treatment per month and 20% received more than 6 h of treatment per month. In terms of treatment duration 20% of the sample received 25 h or less of training, 37% of participants received 26–50 h of training and 43% of the sample received more than 50 h of training.

2.5. UCSD Performance-based Skills Assessment (UPSA; Patterson et al., 2001)

The UPSA was administered at study entry and after the cognitive remediation intervention. This standardized, performance-based instrument of everyday function provides information regarding patients' ability to plan trips to the beach and zoo (recreation planning), count out and provide change using actual domestic currency and write checks for bills (finance), ask for information and reschedule a doctor's appointment via the telephone (communication), plan a bus trip on the local bus system using relevant maps (mobility), and identify items necessary for a recipe that are missing from a simulated pantry (household management). Each of the five subscales was scored on a 1–20 scale, thus summing subtest scores results in a total score on a scale of 0 to 100. Recent studies have supported the ecological validity of the UPSA in patients with a primary psychotic disorder, showing that UPSA performance is closely related to a caretaker measure of physical functioning, personal care skills, interpersonal skills, social acceptability, community activity and work skills (Bowie et al., 2006), as well as actual residential independence (Mausbach et al., 2008).

2.6. Data analysis

Data were evaluated for normality. In no case was there evidence that variables included in the study violated the

assumptions underlying the use of parametric statistical procedures. Within group *t*-tests were used to assess pre- to post intervention change in neurocognitive domains targeted by the cognitive remediation intervention (Working Memory and Processing Speed indices from the WAIS-III), as well as functional capacity (UPSA). We investigated relationships between neurocognitive, symptom and process measures to change in functional status after the intervention in three steps. In the first step we computed partial correlation coefficients between baseline positive and negative symptoms, the process variables of treatment intensity (h/month) and duration (total hours), baseline crystallized verbal ability (Vocabulary subtest of the WAIS-III), sustained auditory attention (Digit Span), verbal learning and memory skills (learning slope and free recall from the CVLT-II), and problem-solving ability (PCET errors) as independent variables and performance-based functional status (UPSA) at the termination of the computer remediation treatment as a dependent measure while controlling for differences in pre-intervention performance-based functional status scores.

In a second step, to help address the issue of multicollinearity among neurocognitive domains, we conducted a multiple regression analysis in which we included baseline performance-based functional capacity measures and all neurocognitive variables in the correlational analysis (independent variables). These variables were entered in a single-step in order to determine which neurocognitive variables measured at baseline explained the most variance in post-intervention measures of functional capacity (the dependent measure), when variance attributable to other neurocognitive variables and baseline measures of functional capacity was controlled.

In the third step, in order to evaluate the relative role of symptoms, treatment process variables and sustained auditory attention as independent variables for predicting change in performance-based functional status across the remediation trial, the dependent measure, we conducted a second multiple regression analysis using a stepwise entry procedure in which baseline performance-based functional capacity scores were entered in a first step, symptoms were entered in a second step, treatment intensity and duration in a third step, crystallized verbal intellectual function in a fourth step and auditory attention and working memory (Digit Span) was entered in a fifth step.

By including baseline measures of performance-based functional status in both regression equations, variance attributable to this measure was removed from post-treatment measures of performance-based functional status. In this way, all observed relationships between neurocognitive, treatment and symptom variables in the regression could be attributed to *change* in performance-based functional status across the 1-year cognitive remediation trial. To facilitate understanding of results, those variables in which higher scores indicated poorer performance or a greater number of symptoms were multiplied by -1 . Alpha was set at .05 and all statistical tests were two-tailed.

3. Results

Relative to scores at study entry, participants showed significant improvement on the Working Memory ($t=3.53$;

Table 2

Partial correlations between clinical and neurocognitive variables at study entry, measures of treatment intensity and duration, and performance-based functioning (total and subtests) at termination of the cognitive remediation intervention controlling for baseline performance-based functioning (total and subtests)

| Variable (Mean +/- SD) | Total | Recreation | Finance | Transport | Comm | House |
|----------------------------------|-------------|------------|---------|-----------|-------|-------|
| Treatment intensity (h/month) | 4.7 (1.7) | -.31 | -.15 | -.16 | -.24 | -.07 |
| Treatment duration (total hours) | 52.6 (28.1) | -.24 | -.41* | -.14 | -.38* | -.12 |
| Positive symptoms PANSS | 18.9 (6.1) | -.14 | -.27 | .00 | -.03 | .22 |
| Negative symptoms PANSS | 19.3 (5.2) | .01 | -.01 | .13 | .04 | -.25 |
| Vocabulary (WAIS-III) | 10.8 (3.6) | .15 | .12 | .38* | .31 | .15 |
| Digit span | 8.9 (3.0) | .40* | .30 | .32 | .28 | .24 |
| Learning slope (CVLT-II) | -.60 (1.4) | .32 | .52* | .16 | .13 | .26 |
| Long delay free recall (CVLT-II) | -1.6 (1.2) | .11 | .35* | .06 | -.04 | -.05 |
| PCET errors | -1.0 (1.4) | .08 | .01 | .11 | .21 | .13 |

Note: UPSA = UCSD Performance-based Skills Assessment; PANSS = Positive and Negative Syndrome Scale; WAIS-III = Wechsler Adult Intelligence Scale; CPT = Continuous Performance Test; CVLT-II = California Verbal Learning Test-II; PCET = Penn Conditional Exclusion Test; Comm = Communication subtest from the UPSA; House = Household Management subtest from the UPSA.

* $p < .05$.

$p < .001$) and Processing Speed indices ($t = 2.67$; $p < .02$) from the WAIS-III. Participants also showed significant improvement on the UPSA ($t = 2.28$; $p < .05$). As can be seen in Table 2, partial correlations controlling for baseline differences in UPSA total and subtest scores showed that Digit Span was the only measure associated with total scores ($r = .40$) on the UPSA after cognitive remediation treatment. Learning slope and free recall scores from the CVLT-II were related to Recreation subtest scores ($r = .52$ and $r = .35$, respectively) but not total

scores. Vocabulary scaled scores were related to the Finance subtest ($r = .38$) of the UPSA, but not total scores. With respect to symptoms, positive symptoms from the PANSS were related to Communication skills ($r = -.39$) but not total scores. With respect to treatment process variables, treatment duration was related to Recreation and Transportation subtests ($r = -.41$ and $r = -.38$, respectively) but not total scores. Treatment intensity was not related to UPSA scores at the termination of remediation intervention.

To further clarify the relationship of baseline neurocognitive test performance to change in functioning after cognitive remediation treatment, we entered baseline performance on the UPSA and all the neurocognitive variables (Digit Span, CVLT-II slope and delayed free recall, and PCET) from our correlational analysis into a multiple linear regression equation. The model, which partitions mutually exclusive components of the overall variance for each variable, explained 53% of the variance in total UPSA scores at the end of the treatment trial ($R^2 = .53$, $F[5,28] = 6.30$; $p < .001$). Higher baseline total scores on the UPSA ($B = .51$, $t = 3.13$; $p < .005$) and higher Digit Span scores from the WAIS-III ($B = .30$, $t = 2.08$; $p < .05$) independently predicted UPSA change scores after treatment when variance from other neurocognitive variables was controlled. Lastly, the results of stepwise regression of baseline functional capacity score (step 1), symptoms (step 2), treatment intensity and duration measures (step 3), vocabulary (step 4) and digit span (step 5) are presented in Table 3. In the first four steps 53% of the variance is explained. With the addition of digit span an additional 9% of variance was explained. In this last step only digit span predicted UPSA at study termination. Thus, here again is evidence of the association between digit span prior to treatment and improvements in post-intervention functional status scores, even when variance for baseline functional capacity measures, symptoms, treatment intensity and duration, and crystallized verbal intelligence were controlled.

Table 3

Results of hierarchical block regression predicting UPSA total score at termination of the cognitive remediation trial

| Variable | B | t-value | p-value |
|---------------------------|------|---------|---------|
| Step 1 ^a | | | |
| Baseline UPSA | .69 | 4.98 | <.001 |
| Step 2 ^b | | | |
| Baseline UPSA | .68 | 4.67 | <.001 |
| Positive symptoms (PANSS) | -.12 | -.88 | .390 |
| Negative symptoms (PANSS) | -.02 | -.13 | .898 |
| Step 3 ^c | | | |
| Baseline UPSA | .57 | 2.48 | .020 |
| Positive symptoms (PANSS) | -.14 | -.82 | .419 |
| Negative symptoms (PANSS) | .03 | .21 | .835 |
| Treatment duration | -.14 | -.51 | .615 |
| Treatment intensity | -.12 | -.58 | .565 |
| Step 4 ^d | | | |
| Baseline UPSA | .53 | 2.17 | .040 |
| Positive symptoms (PANSS) | -.12 | -.73 | .472 |
| Negative symptoms (PANSS) | .05 | .30 | .768 |
| Treatment duration | -.13 | -.45 | .657 |
| Treatment intensity | -.12 | -.55 | .589 |
| Vocabulary | .09 | .52 | .609 |
| Step 5 ^e | | | |
| Baseline UPSA | .45 | 1.96 | .063 |
| Positive symptoms (PANSS) | -.17 | -1.06 | .299 |
| Negative symptoms (PANSS) | .04 | .31 | .759 |
| Treatment duration | -.18 | -.68 | .502 |
| Treatment intensity | -.02 | -.10 | .923 |
| Vocabulary | .02 | .10 | .923 |
| Digit span | .32 | 2.24 | .036 |

Note: UPSA = UCSD Performance-based Skills Assessment (UPSA); PANSS = Positive and Negative Syndrome Scale.

^a $R^2 = .47$, $F = 24.75$, $df = 1, 28$, $p < .001$.

^b $R^2 = .49$, $F = 8.15$, $df = 3, 26$, $p < .005$.

^c $R^2 = .53$, $F = 5.37$, $df = 5, 24$, $p < .005$.

^d $R^2 = .53$, $F = 4.39$, $df = 6, 23$, $p < .005$.

^e $R^2 = .62$, $F = 5.13$, $df = 7, 22$, $p < .005$.

4. Discussion

This is among the first studies, to our knowledge, to investigate the relative role of several domains of neurocognition, symptoms and treatment process variables for prediction of generalization of the effects of cognitive remediation to a measure of performance-based instrumental-life skills. These

results demonstrate in a longitudinal design that neurocognitive skills predicted change in functional status after a one-year course of cognitive remediation in persons with schizophrenia even when variance attributable to symptoms, treatment intensity and duration, and crystallized verbal intelligence was controlled. More specifically, analysis of individual neurocognitive measures showed that auditory sustained attention and working memory was linked to functional status after the cognitive remediation trial and this measure remained a significant predictor of change in functional status even when intercorrelations with other neurocognitive domains were controlled. Measures of positive and negative symptoms, verbal learning and memory, problem-solving, treatment intensity and duration, and crystallized verbal ability were not related to overall change in functional status after outpatient rehabilitation. These findings are particularly salient in that they do not simply suggest a link between neurocognitive skill and functional status, but instead suggest which cognitive skills are most predictive of the ability of patients with schizophrenia to capitalize on cognitive remediation programs consisting of computer-administered, extended drill-and-practice cognitive exercises organized hierarchically from simpler to more complex neurocognitive functions. The observation that the measure of auditory sustained attention and working memory selected for the current study (Digit Span) remained a significant predictor of functional outcome at the end of the remediation trial even after including Vocabulary scaled scores in the stepwise regression model, suggests that these findings were not an epiphenomenon of estimated individual differences in global, verbal IQ.

Studies of predictors of response to cognitive remediation interventions to date in patients with schizophrenia are very small in number and have studied outcome measures that were a component of the remediation intervention itself (Fiszdon et al., 2005), or have used heterogeneous samples that have included people with schizophrenia along with other diagnostic groups (Choi and Medalia, 2005; Medalia and Richardson, 2005). Thus, an important feature of the current findings is that they provide a window on predictors of change as a function of remediation treatment on the ability to conduct basic life-skill tasks that are distal from the site of the remediation intervention in a homogenous sample of patients with schizophrenia/schizoaffective disorder.

One interpretation of the current findings is that impairment in basic sustained auditory attention and working memory interferes with the ability to learn cognitive tasks in cognitive remediation, making acquisition of skills slower and more laborious than patients with less impaired sustained auditory attention. These findings also suggest that the integrity of simple aspects of neurocognition is crucial for acquisition of more complex, multifactorial neurocognitive skills trained in this type of comprehensive, hierarchically organized, sustained remediation intervention.

An important implication of the current results is that they suggest that individuals diagnosed with schizophrenia who receive more than 5 h of cognitive remediation treatment per month do not show greater generalization to measures of everyday life skills than those individuals diagnosed with schizophrenia receiving less than 5 h of treatment per month.

Similarly, individuals diagnosed with schizophrenia treated with over 50 h of cognitive remediation do not show greater benefit than those receiving less than 50 h of treatment. We note that the failure to find effects of treatment intensity or duration on outcome of cognitive remediation in the current report is discrepant from those reported by Choi and Medalia (2005). Two explanations for the source of this inconsistency in findings may be advanced. First, differences in proximity of outcome measures to the cognitive intervention selected for these respective studies may have led to differing results. In the Choi and Medalia study, intensity was linked to performance on a test of clerical skill that was more closely allied with measures of sustained visual attention. Measures of work function, considerably more distal from the site of the cognitive intervention, did not show effects of treatment intensity. Similarly, the performance-based measure of everyday life-skills selected for the present study can be considered moderately distal from the target of the remediation intervention and thus, perhaps, less sensitive to the effects of remediation. Second, variation in treatment intensity was more restricted in the current study (mean=4.7 h/month, SD=1.7) and the vast majority of participants in the current study would have been classified as “low intensity” in that study. Effects of treatment intensity might become evident with a subsample of patients receiving higher intensity treatment.

We also note that the failure to find relationships between treatment intensity and outcome in the current study is inconsistent with findings from the literature on Integrated Psychological Therapy (IPT) for schizophrenia which includes cognitive remediation as a crucial element of treatment (e.g., Roder et al., 2006). Again, this discrepancy may be explained by the wider range of treatment intensity evident in those studies.

Several caveats to the current findings should be noted. First, the results of this study are of a group that provides guidance on *which* neurocognitive variables may be linked to change in functional status as a result of remediation, rather than *how* these variables impact functional status (i.e., whether sustained auditory attention has a direct or indirect effect on change in functional status). Larger sample sizes, coupled with the inclusion of additional, potential mediating variables, would be necessary to address these questions. Second, some clinical researchers argue that meaningful clinical change on an outcome variable occurs when performance is elevated to a level after treatment that is indistinguishable from healthy controls (e.g., Kendall and Grove, 1988). The absence of data on the UPSA from a demographically-matched, healthy control group precluded measurement of task normalization. Third, the current sample size of 36 participants is modest for a multiple regression analysis, and important relationships between study variables and changes in performance-based functioning as a result of rehabilitation may have been overlooked as a consequence. Fourth, cognitive remediation was not offered as a stand-alone treatment, but was administered as part of a more generalized outpatient rehabilitation program that included group therapy and daily goal formulation, as well as vocational counseling, exercise and individual therapy. Thus, as an observational study, predictors of change in functional capacity in this treatment trial could be linked to these other interventions in addition to

cognitive remediation. Lastly, measures of performance-based everyday life skills have been criticized for serving as simply more ecologically-valid measures of neurocognitive skill, and thus links between neurocognitive skill and these measures may represent an artifact of method variance. Nonetheless, we note that while performance-based measures of everyday life skills undoubtedly require a host of neurocognitive skills, including sustained attention, memory and problem-solving, we have documented a selective relationship between only one aspect of neurocognition, auditory sustained attention and working memory, and the relationship was not with absolute level of everyday life skills but rather in change in everyday life skills over the course of a specific intervention. In summary, these results emphasize the importance of baseline auditory sustained attention and working memory as a predictor of acquisition of everyday life-skills for patients with schizophrenia enrolled in sustained programs of outpatient cognitive rehabilitation.

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Contributors

Matthew M. Kurtz, PhD, was involved in the initial conceptualization of the study and design, oversaw administration of the intervention, and all data collection efforts, helped formulate the data analytic plan, analyzed resultant data and wrote all components of the first draft.

James C. Seltzer, PhD, was involved in initial conceptualization of the study and made intellectual contributions to the study design and the remediation intervention specifically.

Marco Fujimoto, BA, was involved in data collection, preparation of data for analysis, conduct of analyses and made contributions to the final draft.

Dana Shagan, PsyD, oversaw data collection, managed administration of the intervention, made intellectual contributions to the development of the remediation intervention and commented on drafts of the manuscript.

Bruce E. Wexler, MD, was involved in initial conceptualization of the study and design, helped formulate the data analytic plan and made extensive intellectual contributions to the remediation intervention and the final text of the article.

Conflict of interest

There are no conflicts of interest.

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