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Improved cognitive function in schizophrenia after one year of cognitive training and vocational services

Tamasine C. Greig [a,*], Wayne Zito [a], Bruce E. Wexler [a], Joanna Fiszdon [a,b], Morris D. Bell [a,b]

[a] *Yale University School of Medicine, Department of Psychiatry, USA*
[b] *VA Connecticut Healthcare System, USA*

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Abstract

A year-long program of Neurocognitive Enhancement Therapy (NET) was used to remediate cognitive deficits in people with schizophrenia who were participating in a vocational program. Seventy-two stable outpatients with schizophrenia or schizoaffective disorder, recruited from an urban community mental health center were randomly assigned to a twelve-month vocational program (VOC) or NET+VOC. The vocational program had characteristics of individual placement and support (IPS) programs but also included transitional funding. NET included computer-based cognitive training exercises, a social information processing group and a work feedback group. Sixty-two participants completed a neuropsychological test battery before and after treatment. After one year of treatment, participants receiving NET+VOC had significantly greater improvements on measures of executive function and working memory than did participants in the VOC only condition. Augmenting vocational services with a multifaceted cognitive remediation program may improve cognition in participants with schizophrenia or schizoaffective disorder.

Keywords: Schizophrenia; Vocational; Cognitive training; Cognitive impairments

1. Introduction

Cognitive impairment is a central feature of schizophrenia that limits recovery. (Green, 1996). Cognitive training using computer-based exercises, individual instruction or group techniques, is a non-pharmacological approach for improving cognitive impairments in schizophrenia (Velligan et al., 2006). Reviews and meta-analyses of various cognitive training programs provide evidence for the effectiveness of cognitive training (Twamley et al., 2003; Kurtz et al., 2007). Cognitive training has been shown to improve sustained attention and language processing (Wexler et al., 1997), executive function (Bell et al., 2001, Wykes et al., 1999), affect recognition (Bell et al., 2001), verbal memory (Hogarty et al., 2004; McGurk and Mueser, 2004), working memory (Bell et al., 2001; Kurtz et al., 2007), processing speed (Hogarty et al., 2004) and social problem solving (Kern et al, 2005).

Several researchers have explored whether cognitive training improves vocational outcomes. McGurk et al.

* Corresponding author.
E-mail address: tamasine.greig@yale.edu (T.C. Greig).

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(2007) report that participants whose supported employment program was enhanced by a cognitive training program called "Thinking Skills for Work", which included computer-based cognitive remediation and a follow-through procedure that addressed cognitive issues in the workplace, achieved competitive employment at a much higher rate than their peers who received traditional supported employment services only. Vauth et al. (2005) randomized inpatients to three conditions in addition to hospital-based vocational services. Participants in the Computer Assisted Cognitive Strategy Training (CAST) condition, which is based on the principles of errorless learning and consists of practicing cognitive strategies in role-plays and on computer tasks, showed greater improvement on measures of attention and verbal memory and demonstrated higher job placement levels at twelve-month follow-up. Bell et al. (2001) found that when Neurocognitive Enhancement Therapy (NET), described below, was added to work therapy, clients worked more hours during a six-month follow-up period. Results also showed that participants who responded to the cognitive intervention by achieving normal levels of function on a memory task had the best work outcomes.

Neurocognitive Enhancement Therapy (NET) is a comprehensive cognitive remediation program consisting of computer-based cognitive training, a social information processing group, and, because the cognitive remediation program is embedded in a vocational program, a work feedback group (Bell et al., 2001). In a randomized clinical trial at a VA Medical Center work therapy program, people in the NET + Work Therapy condition showed greater improvement in executive function, working memory and affect recognition after 6 months of treatment than those in the work only condition (Bell et al., in press).

Given the functional significance of cognitive deficits in schizophrenia and their persistence after pharmacotherapy (Bellack et al., 2004), replication and further development of NET and related treatments is warranted. The present study was undertaken to replicate and build upon the Bell et al. (2001) study in several ways. It was designed to help participants obtain work in the community rather than work placements in a medical center, the intervention was one year rather than six months, and participants were drawn from an urban community mental health center rather than a VA population. We predicted that results would replicate our previous findings, with NET participants demonstrating greater performance gains on measures of executive function, working memory and affect recognition than those participants receiving vocational services only.

2. Method

2.1. Participants

Seventy-two stable outpatients with schizophrenia or schizoaffective disorder were the intent-to-treat sample in a one-year study of vocational and cognitive rehabilitation at a large urban mental health clinic. Research staff conducted brief presentations for the treatment teams that served people with schizophrenia or schizoaffective disorder. Clinicians then approached their clients and asked if they were interested in participating in the study. People who were interested in participating were invited to a brief, informal information meeting. Approximately 120 people attended information sessions over the course of the four-year recruitment phase; 88 signed consent forms, 77 were randomized and 5 were subsequently excluded for cause. Of the 72 in the intent-to-treat sample, 62 (86%) completed all procedures. The remaining 10 participants were contacted but declined follow-up testing. These 10 did not differ on background, illness or neuropsychological measures at intake from those who completed follow-up.

Participants met diagnostic criteria based on the Structured Clinical Interview for Diagnosis (SCID; Spitzer et al., 1997) and were eligible if they were clinically stable (i.e., GAF > 30, no housing changes, psychiatric medication alterations, or psychiatric hospitalizations in the 30 days prior to intake), had no history of head trauma and had not abused substances for 60 days prior to intake. All participants expressed a desire to work and were paired with job specialists during intake with the goal of quickly obtaining employment.

Of the 62 participants, 29 were women, 30 were white and 39 were African American. Forty-one were diagnosed with schizophrenia and 21 with schizoaffective disorder. Their mean age was 40, mean IQ 87 and average age at first hospitalization 24. The majority (61%) were on atypical medication. No significant differences in demographic or symptom variables were found between the two conditions. (See Table 1).

2.2. Methods

After obtaining written informed consent approved by the institutional review board, research psychologists collected demographic information, conducted clinical interviews, and administered neuropsychological tests (at intake and at one-year follow-up). Testing was typically completed over the course of several weeks in sixty-minute sessions. Tests were selected because they were found to be stable at test and retest (10 week

Table 1
Participant characteristics

	VOC (*N*=29)		NET+VOC (*N*=33)	
	n	%	*n*	%
Gender				
Male	14	48	19	58
Female	15	52	14	42
Ethnicity				
African American	13	45	16	49
Asian	0	0	1	3
Caucasian	15	52	15	45
Hispanic	1	3	1	3
Schizophrenia diagnosis				
Paranoid	12	41	17	52
Undifferentiated	2	7	3	9
Disorganized	3	10	2	6
Residual	1	3	1	3
Schizoaffective	11	38	10	30
Medications				
Atypical	17	59	21	64
Conventional	8	28	5	15
Both	4	13	7	21
	Mean	SD	Mean	SD
Age	37.69	9.14	42.73	9.41
Education	12.50	1.84	12.95	2.59
WAIS IQ	84.48	16.17	89.42	15.57
Age at 1st hosp	22.28	5.54	25.64	9.27
Lifetime # hosp	8.18	6.57	9.42	9.20
PANSS				
Total	81.72	10.97	77.48	15.84
Positive	18.17	4.59	17.67	4.85
Negative	21.55	6.84	19.85	6.46
Cognitive	20.17	4.52	19.03	5.22
Hostility	9.17	3.13	8.03	2.67
Emotional discomfort	10.54	4.18	10.27	3.32

No significant differences by condition.

interval) in a schizophrenia population (Greig et al., 2004a).

Following intake testing, participants were stratified based on cognitive impairment and work experience and were randomly assigned to 1 year of either NET+VOC or VOC only. Participants were classified as cognitively impaired if they scored 1 SD below the mean (for a previously established schizophrenia sample) on 2 or more of 6 neuropsychological indicators (Bell et al., 2001). Participants were classified as work experienced if they had ever held a continuous full-time job for at least one year. A statistical assistant not associated with the study performed random assignment using computerized random numbers obtained from a website.

2.2.1. Outcome measures

Cognitive function was evaluated with categories complete, conceptual level and total errors on the Wisconsin Card Sorting Test (WCST, (Heaton, 1981), the Digit Span and Letter Number Sequencing subscales of the WAIS-III (Wechsler, 1997a), the Logical Memory I and II and Visual Reproduction I and II subscales of the Wechsler Memory Scale, III (WMS-III; Wechsler, 1997b), the Trial 1-3 total and thirty-minute recall scores from the Hopkins Verbal Learning Test, Revised (HVLT-R; (Brandt and Benedict, 2001) and the Gorham's Proverb's Test (Gorham, 1951) rated for bizarreness (Marengo et al., 1980). Social cognition was assessed with the North American version (Greig et al., 2004b) of The Hinting Task (Corcoran et al., 1995) and the Bell-Lysaker Emotion Recognition Task (BLERT; Bell et al., 1997).

2.2.2. Conditions

Participants in both conditions received identical vocational services (Greig et al., 2004c) that shared some of the tenets of IPS (Bond et al., 2001) and received a score of 62 out of 75 on the IPS fidelity scale (Bond et al., 1997) when rated by three trained raters, including Gary Bond, who interviewed the program staff and the two vocational specialists (Gary Bond Ph. D, personal communication). The vocational program differed significantly from IPS in that the job specialists were not part of the treatment team and transitional funds were available to allow people get to work quickly and "prove themselves" before being hired by the employer. All participants worked in competitive settings in the community.

Participants in the VOC condition also attended two staff-led groups: a work support group and a lifestyles group. The work support group consisted of general discussion of work-related issues. The lifestyles group focused on social concerns (including how to handle their newfound income), but without structured exercises or planned activities in order to preserve the distinction of the VOC condition as a non-cognitive intervention. Participants were paid minimum wage for each hour-long group attended. VOC participants had a mean of 28.7 (14.98) work support groups and a mean of 23.72 (14.12) life-style groups for a combined mean of 52.4 (27.25) groups for the year.

Participants in NET+VOC received identical vocational services augmented by computer-based cognitive remediation for up to 10 h per week for one year, receiving minimum wage for each hour completed. They averaged 125.93 h (SD=91.78) of cognitive training, over an average of 34 weeks (SD=15.71), for an

average weekly training of 3.92 h (SD=1.94). We deliberately planned for this high level of training intensity and duration, even though we were concerned that it might conflict with work hours. We did so because NET is based upon models of neuroplasticity that call for intense and repetitive practice in order to remediate cognitive deficits.

Cognitive remediation exercises were drawn from two sources: CogRehab (Bracy, 1995), originally developed for people with compromised brain function and modified according to our specifications for people with schizophrenia, and Sci-Learn, developed by the Scientific Learning Corporation (Scientific Learning, 2003) in conjunction with one of the senior authors (BEW, www.hypomania.scilearn.com, 2003). The exercises targeted cognitive abilities compromised in schizophrenia (e.g., attention, language, memory, executive function), and followed a standard sequence and progression of difficulty. Participants graduated to new tasks after achieving a prescribed performance level, or when their performance remained unchanged over 8 half-hour training sessions. In this way, tasks were kept challenging but not too frustrating, and the intervention was adjusted to each person's pattern of cognitive strengths and weaknesses.

In addition to cognitive remediation, people in the NET+VOC condition attended weekly work feedback and social information processing groups. Job specialists attended the work feedback group and provided participants with specific feedback based on the Work Behavior Inventory (WBI; Bryson et al., 1997) and the Vocational Cognitive Rating Scale (VCRS, Greig et al., 2004a). Job specialists completed biweekly WBI and VCRS ratings after brief workplace observation and interviews with supervisors. All participants who were working were rated on the WBI and VCRS, but only those in the NET+VOC condition received feedback. NET+VOC participants also attended the social information-processing group using exercises designed by Ben-Yishay et al. (1985) in which participants were taught to give presentations to each other on topics about work, ask questions, and give detailed feedback and constructive criticism. Both groups demanded attention, memory, and problem solving, as well as affect recognition, empathy, and verbal communication skills. As in the VOC condition, participants received minimum wage for each group attended. NET+VOC participants had a mean of 29.8 (14.2) work feedback groups and a mean of 22.3 (14.9) social information processing groups for a combined mean of 52.2 (25.74) groups for the year. Conditions did not differ significantly on number of groups attended (df=61, t=.04, p=n.s.).

Table 2
Means and standard deviations at intake and follow-up

	VOC (n=29)				NET+VOC (n=33)			
	Intake		1 Year F/U		Intake		1 Year F/U	
	Mean	(SD)	Mean	SD	Mean	SD	Mean	SD
Executive function factor								
WCST errors	78.28	22.37	79.48	23.33	79.15	17.47	85.24	17.18
WCST % concept level*	79.59	22.57	79.52	23.44	79.82	17.62	86.55	16.96
WCST categories*	2.97	2.66	2.66	2.72	3.09	2.32	3.94	2.10
Working memory factor								
WAIS L/N	7.38	3.59	7.43	3.76	8.0	2.68	7.85	3.57
WAIS DS*	8.45	3.26	8.46	2.80	8.94	2.35	9.82	2.40
Visual and verbal memory factor								
WMS VRI	5.93	3.61	6.79	4.03	7.18	3.71	8.03	3.76
WMS VRII	8.03	3.35	8.41	3.23	9.06	2.73	9.94	2.62
HVLT total	17.72	6.00	20.17	5.69	19.42	5.50	20.36	4.34
HVLT recall	6.14	2.91	6.72	3.29	6.45	2.67	7.09	2.14
Social cognition factor								
Hinting Task	15.55	4.29	16.24	3.71	15.97	3.05	17.62	2.39
BLERT	13.07	4.86	13.32	4.38	14.03	3.63	15.19	3.11
WMS LMI	6.55	3.62	7.55	3.62	7.45	2.89	9.18	3.09
WMS LMII	7.86	3.53	8.93	3.45	8.45	2.90	9.94	2.64

* p<01.

3. Data analysis

Normality of distribution was determined for each variable and Blom transformations performed when necessary. The intent to treat analysis included all participants who were randomized, regardless of their level of participation. As a data reduction strategy, a factor analysis of intake neuropsychological data was performed. Principal components analysis followed by varimax rotation of intake data generated 4 factors: executive function, working memory, visual and verbal memory, social cognition. Multivariate analysis of variance (MANCOVA) were performed on follow-up scores with intake scores used as covariates using variables from each factor (see Table 2). Conditions were compared on demographic variables using chi square analysis for frequency and alpha was set at .01. All other analyses were parametric, two tailed, with alpha set at .05.

3.1. Results

MANCOVA of executive functioning variables indicated an overall significant effect for condition ($F(3,56)=4.41$, $p<.01$). At 12 months, the NET+VOC condition scored significantly higher on WCST categories complete ($F(1,58)=9.63$, $p<.01$) and WCST percent conceptual level scaled score ($F(1,58)=5.79$, $p<.01$). MANCOVA on working memory variables indicated an overall significant effect for condition ($F(2,57)=3.13$, $p<.05$). Digit span was the only individual variable to reach significance in the analysis ($F(1,58)=6.09$, $p<.01$ with the NET+VOC condition demonstrating better scores. MANCOVAs on verbal/visual memory and social cognition factors did not reveal overall significant condition effects ($F(4,53)=.738$, $p=.57$ and $F(4,51)=1.83$, $p<.14$).

4. Discussion

These results are similar to those of Bell et al. (2001). The factor structure of the baseline neuropsychological measures was largely the same as in the previous sample, the same two factors yielded significant treatment effects, and the largest effects were in the same individual measures. Both studies found that participants who received NET showed significantly greater gains in categories complete and conceptual level on the WCST and in Digit Span. Greater improvement in affect recognition after one year was not found for NET+VOC, in contrast to the Bell et al. (2001) findings of improved affect recognition after 6 months of NET plus work therapy. However, analysis of the one-year follow-up data from the Bell et al. (2001) VA study, indicate that affect recognition improvement was no longer significant (Bell et al., in press). It may be that the six-month improvement was an unstable finding.

To our knowledge, NET is the first treatment for cognitive deficits in schizophrenia to show significant benefit in two randomized controlled trials with moderate to large samples. Given the prevalence, functional significance and persistence after pharmacotherapy of cognitive deficits in schizophrenia, this replication of the benefits of NET provides support for continued development and evaluation of cognitive remediation treatments. Further analyses of these data will evaluate the persistence of benefit after treatment and effects on work outcomes.

NET included both computerized cognitive remediation and cognitively-focused weekly groups. In addition, most patients participated in work. We cannot determine the relative contribution of each of these activities to observed benefits, and they may work synergistically. However, a recent study, using some of the same computer exercises employed in this study, also found that the patients receiving the exercises showed greater improvement on Digit Span than did a comparison group (Kurtz et al., 2007). Since that study did not include additional groups or employment in the intervention, it suggests that the most important factor in the present results may be the computerized cognitive remediation.

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Contributors

Drs Bell and Wexler designed the study. Drs Bell, Wexler, Greig and Zito contributed to the writing of the protocol. Dr. Greig wrote the first draft of this manuscript. Dr. Zito conducted the statistical analysis for this report. All authors contributed to and have approved the final manuscript.

Conflict of interest

Dr. Wexler was a consultant to SciLearn (a company that made one of the cognitive training programs that we used). All other authors declare that they have no conflict of interest.

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