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Psychiatry Research 125 (2004) 1–7

PSYCHIATRY
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Durability of cognitive remediation training in schizophrenia: performance on two memory tasks at 6-month and 12-month follow-up

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Received 17 January 2003; received in revised form 19 September 2003; accepted 23 October 2003

Abstract

Patients with schizophrenia have consistently been found to exhibit cognitive deficits, particularly in memory, which have been suggested to mediate functional outcomes. Several recent reviews of cognitive retraining have concluded that these deficits respond to training, although the sustainability of cognitive improvement following completion of training has not been adequately evaluated. Most studies had small samples and very short follow-up periods. As part of a larger study, we examined performance on two memory tasks in two groups of participants: those who received computerized cognitive remediation training in addition to work therapy ($n=45$), vs. those who only received work therapy ($n=49$). Computerized cognitive remediation included hierarchical training on a computerized digit span task and a computerized words serial position task. Assessments using the same computerized tasks were made at three time points: baseline, end of active intervention, and 6-month follow-up. Compared to the active control condition (work therapy only), the group receiving computerized cognitive remediation in addition to work therapy showed significantly greater improvements on the trained digit span task following training. These improvements were maintained at the 6-month follow-up. There were no significant group differences on the word serial position task at any time point. Results indicate that computerized training can lead to sustained improvements on some, but not all, training tasks.

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Keywords: Cognitive rehabilitation; Cognition; Digit span; Serial recall; Span of apprehension

1. Introduction

In the past decade, there has been a resurgence of interest in the remediation of cognitive deficits

in schizophrenia. Improved cognitive function (e.g. better memory and attention) may lead to improved life quality, and has been reported to correlate with self-esteem (Wykes et al., 1999). Improved cognitive function may also lead to enhanced efficacy of other psychosocial interventions (e.g. skills training, medication management), in turn leading to better functional outcome.

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A series of studies and reviews indicates that cognitive function is correlated with functional outcome, including interpersonal, occupational and social problem-solving skills (Green, 1996; Green et al., 2000; Mueser et al., 1991; Silverstein et al., 1998). The bulk of the research has been promising, indicating that cognitive impairments can be rehabilitated. Following training, patients with schizophrenia perform significantly better on the trained tasks (Kern et al., 1996; Stratta et al., 1994), and there is some evidence that improved performance on trained tasks generalizes to other, non-trained tasks (Bell et al., 2001; Bellack et al., 2001; Cassidy et al., 1996; Corrigan et al., 1995; Medalia et al., 1998, 2001; van der Gaag et al., 2002; Wykes et al., 1999). Very few studies, however, have examined the durability of cognitive improvements once the cognitive remediation training concludes.

Although cognitive remediation programs vary considerably, all include a practice component, where the trainee practices tasks associated with a particular cognitive function (e.g. story recall for memory). In addition to practice, some programs also incorporate specific training of strategies (e.g. mnemonics, semantic clustering), increases in task difficulty, contingent reinforcement, and corrective feedback. Only a handful of cognitive remediation studies have included a follow-up assessment to evaluate the durability of improvement observed after training.

Several studies have specifically examined the durability of gains made following training on the Wisconsin Card Sorting Task (WCST). Training improvements have been documented to persist at 1-day (Bellack et al., 1990), 2-week (Vollema et al., 1995), 4-week (Kern et al., 1996) and 6-week (Metz et al., 1994) follow-ups. Durability of training effects has also been reported to persist at a 48-h follow-up for social processing tasks (Corrigan et al., 1995), and at a 1-week follow-up for a span of apprehension task (Kern et al., 1995). Conversely, a lack of memory training effects has also been reported at a 4-week follow-up (Medalia et al., 2000).

Two studies in the recent literature indicate that training improvements may be long-lasting. Wexler and colleagues (Wexler et al., 1997) reported that

for 11 out of 22 schizophrenia patients in their study, gains made during a 10-week cognitive training program targeting sustained perceptual, memory and motor tasks were maintained at a 6-month follow-up. Similarly, Wykes and colleagues (Wykes et al., 2003) reported that a course of comprehensive cognitive remediation training administered to 17 patients with schizophrenia resulted in non-trained memory task improvements that were sustained at a 6-month follow-up.

The above studies are encouraging and suggest that the effects of cognitive remediation training in schizophrenia are maintained once the training is withdrawn. However, any conclusions drawn from these reports should be tempered given the small number of studies, frequently short follow-up periods and small sample sizes.

Although improved cognitive function may lead to immediate effects as far as increased self-esteem and life quality, it is unlikely that it readily translates into improved long-term outcomes. As suggested by some (e.g. Green et al., 2000), it is more likely that improved cognitive function helps patients to benefit from other psychosocial interventions, such as skills training and psychoeducation. This, in turn, suggests that any improvements in cognition that result from cognitive remediation need to be durable—not just for days or weeks, but more likely for months and years, as patients continue to receive various therapeutic interventions. The current study examines the durability of performance improvements on two memory tasks, 6 and 12 months following the inception of cognitive remediation training.

2. Methods

2.1. Participants

Participants were outpatients diagnosed with schizophrenia or schizoaffective disorder who had taken part in an ongoing study of work therapy with or without cognitive remediation training (see Bell et al., 2001, for details). Written informed consent was obtained for all participants. All diagnoses were made using the Structured Clinical Interview for DSM-IV (SCID-IV, First et al., 1996), administered by a Ph.D.-level psychologist.

In order to enter the study, all participants had to meet the following criteria: Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV, American Psychiatric Association, 1994) diagnosis of schizophrenia or schizoaffective disorder; no change in psychiatric medications in the past 30 days; no change in housing in the past 30 days; no substance abuse in the past 30 days; no documented neurological disorder or developmental disability; and Global Assessment of Function score over 30. All participants were referred to the study by their clinicians, and all were receiving treatment either at the VA Connecticut Healthcare System or at the Connecticut Mental Health Clinic. From the 132¹ individuals who entered the study and had reached the 12-month follow-up assessment, full intake, 6-month, and 12-month follow-up data were available for 94 persons.² Within this sample, 64 individuals were diagnosed with schizophrenia (nine disorganized, 46 paranoid, seven residual, two undifferentiated), and 30 individuals were diagnosed with schizoaffective disorder. Participants were randomly assigned to one of the two conditions: work therapy only (WT only; $n=49$) or work therapy plus Neurocognitive Enhancement Therapy (WT + NET; $n=45$). Both conditions are described in Section 2.3. Demographic information for both groups is presented in Table 1.

2.2. Computerized cognitive remediation tasks

All computerized cognitive remediation tasks were modifications of the Psychological Software Services CogReHab Software (Bracy, 1995), a multi-media, Windows-based software designed for use with traumatic brain injury and other neurological impairments resulting in compromised cognitive function. The following tasks, which were administered to all schizophrenia patients at intake, and at 6-month and 12-month follow-up, are the focus of the current study:

¹ A total of 152 participants have been entered into the study; however, only 132 have reached the 12-month follow-up stage.

² There were no demographic (age, gender, education, lifetime hospitalizations, WAIS FSIQ, PANSS total) differences between the 94 individuals included in the study and the 38 individuals excluded due to incomplete data.

Table 1
Demographics for 'NET+WT' and 'WT only' groups

Variable	'NET+WT'	'WT only'	Significance	
	$n=45$ M (S.D.)	$n=49$ M (S.D.)	t or χ^2	P -value
Age	41.9 (9.9)	43.2 (8.0)	-0.71	0.48
Education	13.3 (2.1)	13.5 (2.2)	-0.50	0.62
Life hosp.	8.6 (13.3)	9.6 (8.9)	-0.41	0.68
WAIS FSIQ	89.3 (13.4)	89.2 (13.3)	0.03	0.97
Gender (male)	34 (76%)	39 (80%)	0.22	0.64
PANSS (total)	78.9 (15.9)	77.8 (12.4)	0.37	0.71
Hand (right)	38 (84%)	40 (82%)	0.91	0.64

2.2.1. Digits sequenced recall

For this digit span task, examinees are presented with digits, flashed one at a time on a computer screen (list length starts with two digits and increases with success). Exposure to each digit is 1.5 s, and there is a wait time of 5 s before recall can start. Following list presentation, examinees are instructed to press corresponding numbered tabs, replicating the sequence of digits. A total of 10 trials are administered. Longest string of digits successfully recalled, and total number of digits successfully recalled are recorded.

2.2.2. Words sequenced recall

For this serial position task, a list of words is presented on the computer screen. The list can be likened to a shopping list, in that words are listed vertically, one per line. List length starts with two words and increases with success. Exposure to the word list is 3 s per word, and there is a wait time of 5 s before recall begins. Following list exposure, examinees are shown one of the list words and asked to indicate its serial order by pressing the corresponding numbered tab. All of the words are types of animals, and all words consist of four letters (e.g. bear, goat, duck). A total of 10 trials are administered. Longest word list with successful recall is recorded.

2.3. Procedure

Upon entry into the study, patients were stratified according to intake cognitive function (see Bell et al., 2001, for details), and randomly assigned to one of the two conditions: work

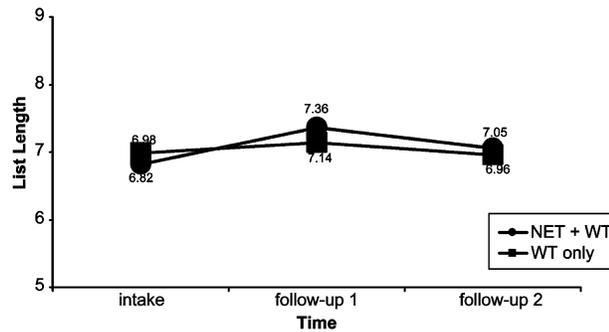


Fig. 1. Word longest list length successfully recalled, by condition.

therapy only (WT only) or work therapy plus Neurocognitive Enhancement Therapy (WT+NET), each lasting 6 months. The work therapy consisted of up to 20 h per week at job placements around the VA, along with a weekly worker's group. NET consisted of up to five 45-min computerized cognitive remediation sessions per week, along with a weekly goal-setting group. Whereas participants in the WT only group could work up to 20 h per week, participants in the WT+NET group could work up to 15 h per week, and could participate in up to five computerized remediation sessions per week. Computerized training followed the drill and practice model, with task difficulty increased based on performance. Participants practiced a variety of tasks tapping different types of memory, attention, reaction time, inhibition, planning and problem-solving. Tasks were presented in visual and auditory modalities. As part of NET, participants also trained on the digits and words sequenced recall tasks. On average, patients in the WT+NET group completed 48 cognitive training sessions (S.D.=32.7, range=2–114). At intake, at the end of the 6-month active phase (F1), and 6 months after the end of the active phase (F2), all participants completed additional assessments, which included the computerized digits sequenced recall and words sequenced recall tasks. Analyses were based on an intent-to-treat model, with individuals receiving minimal intervention (whether work or computerized training) retained in both the WT only and the WT+NET groups. This strategy was chosen because it decreases the like-

lihood of sample bias and Type I error. Post-hoc analyses examined the relationship between number of training sessions and changes in performance, as well as symptomatology and changes in performance.

3. Results

Figs. 1 and 2 show performance on the digits and words recall tasks at intake, F1 and F2 for the WT only and the WT+NET groups.

We performed a repeated measures multivariate analysis of variance (MANOVA), between conditions (WT only vs. WT+NET), with total number of digits recalled, longest digit list length, and longest word list successfully recalled as the dependent variables, and intake, F1 and F2 as the three time points. The overall analysis was significant for time by condition, $F(6, 132)=4.707, P<0.001$. There was a main effect of time for total number of digits recalled, $F(2, 182)=15.215, P<0.001$, and a main effect of time for longest digit list length, $F(2, 182)=9.924, P<0.001$, with scores improving over time. There was no main effect of time for longest word list, $F(2, 182)=2.176, P=0.116$. There was a time by group interaction for total number of digits recalled, $F(2, 182)=7.842, P<0.005$, and for longest digit list length, $F(2, 182)=13.878, P<0.001$.

Next, we performed analysis of covariance (ANCOVA), comparing the two groups at F1 and F2 assessments, partialling out intake scores. There

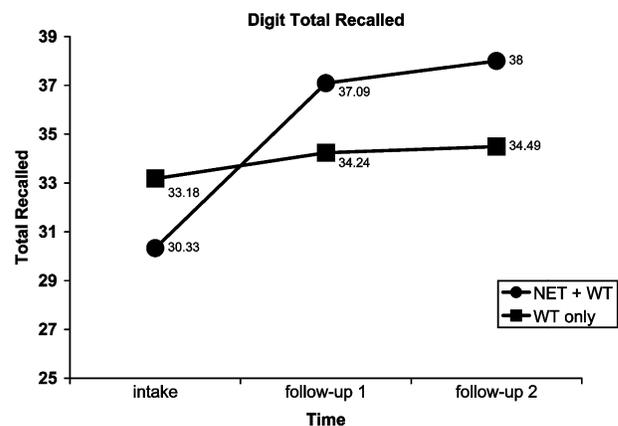


Fig. 2. Total of digits recalled, by condition.

was a significant difference for total number of digits recalled both at follow-up 1, $F(1, 91) = 6.40$, $P < 0.05$, as well as follow-up 2, $F(1, 91) = 9.93$, $P < 0.005$, with the WT+NET group outperforming the WT only group. There was also a significant group difference at F1, $F(1, 91) = 14.4$, $P < 0.0005$, and F2 $F(1, 91) = 11.08$, $P < 0.005$, for longest digit list length, with the WT+NET group outperforming the WT only group. There were no significant group differences on the longest word list variable.

As post-hoc analyses, we examined the influence of symptoms and number of training sessions on post-training changes in task performance. We computed Pearson correlations between number of training sessions and the following variables: number of digits recalled difference score between F2 and F1 ($r = -0.002$; $P = 0.99$); and longest word list recalled difference score between F2 and F1 ($r = 0.238$; $P = 0.12$). We also computed Pearson correlations between total PANSS (Positive and Negative Syndrome Scale) score at the end of the active phase and the following: number of digits recalled difference score between F2 and F1 ($r = 0.167$; $P = 0.27$); and longest word list recalled difference score between F2 and F1 ($r = -0.084$; $P = 0.58$).

4. Discussion

In the current study, we examined the effects of cognitive remediation training on memory performance in schizophrenia. Compared to an active control condition (WT only), the group receiving cognitive remediation training (WT+NET) showed significantly greater improvements on a computerized memory task (digits sequenced recall) following training. More important, these gains were maintained 6 months after the conclusion of training. Post-hoc analyses indicate that neither total symptom level nor number of training sessions was associated with post-training changes in performance.

Whereas a number of studies of cognitive remediation have shown improved performance on trained tasks, few studies have addressed the issue of long-term durability of such improvements. Results of the current study suggest that improve-

ments on cognitive tasks that occur as a result of training are sustained over prolonged periods of time. This is important, as the aim of cognitive rehabilitation is to elicit long-term changes in cognition, which in turn may increase the benefits of other therapeutic interventions and lead to improved functional outcomes.

There are several potential explanations for the durability of training effects. The fact that gains made during a simple drill and practice task were sustained at 6 months after the intervention was discontinued suggests more than a simple practice effect. It is possible that, without specific instruction in such, the participants learned and adapted memory enhancement strategies (e.g. chunking) that aided them in subsequent recall. It is also possible that the laboratory-based training on the digit span task resulted in durable improvement because this skill was further practiced in the real world, both during the training, as well as during the follow-up period. Patients are frequently called on to remember number-based information such as appointment dates, phone numbers, and identification numbers, and it may have been this continued exposure and practice that was responsible, in part or in whole, for the observed results.

Although the finding of durable improvement on the trained digits sequenced recall task is encouraging, it is still uncertain whether the durability of improvement is limited to the specific task being trained or whether it would also be observed on similar but non-trained, tasks, a point raised by critics of the drill and practice remediation approach (e.g. Wilson, 1998). This point certainly holds merit; however, relying only on non-trained tasks as measures of training success would make the interpretation of negative results difficult, as one would not know whether they are due to the lack of intervention efficacy or the lack of generalizability. In a previous report (Bell et al., 2001), we noted that at the conclusion of training there was generalizability to non-trained tasks. We are currently in the process of analyzing additional data to determine whether these improvements are sustained over time.

Performance on the computerized words serial position task did not improve following training. This is somewhat surprising, particularly since

there were significant improvements on the digits task, and both tasks rely heavily on immediate memory. However, even though both tasks may superficially appear similar, the words serial position task is substantially more challenging. Whereas the digit sequenced recall task allows for use of strategies such as chunking to decrease memory load while at the same time allowing for greater digit spans, the words serial position task is not amenable to such mnemonic strategies. Another difference between the two tasks is that the digit span task is essentially a symbol encoding task, whereas the words serial position task is a lexical task. Lexical tasks involve language processing that may require different neural pathways than those used for symbol encoding. Also, whereas the digit span task is a relatively pure task of immediate memory, the word serial position task requires both immediate memory and sequencing processes. Finally, the two tasks can also be argued to differ as far as real-world applicability, and patients may have had additional exposure to and practice with number recall (e.g. remembering phone numbers), but not word serial position recall.

The current study provides encouraging results regarding the long-term durability of cognitive remediation training. At the same time, the current study also invites many questions regarding the limits of laboratory-based cognitive remediation training. Performance on one measure of immediate memory improved as a result of training, and remained significantly better at a 6-month follow-up. In contrast, performance on another measure of immediate memory did not change as a result of training. This inconsistency highlights how little we know about cognitive remediation strategies, how they work, and what their limits are. It is possible that certain tasks are more amenable to the type of drill and practice training described herein, whereas other tasks require a more holistic approach. As suggested earlier, the observed differences in intervention efficacy may also be due to the higher difficulty level for the word serial position task, which would suggest the need for more rigorous evaluations of training gains as a function of task difficulty. In addition to these issues, future studies will also need to continue exploring the generalizability of training effects

and subsequent improvements in functional outcome.

Acknowledgments

This research was funded by the Department of Veterans Affairs, Rehabilitation Research and Development Service (#D2356-R).

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