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Remediation of memory disorders in schizophrenia

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ABSTRACT

Background. Memory deficits are commonly experienced by patients with schizophrenia, often persist even after effective psychotropic treatment of psychotic symptoms and have been demonstrated to interfere with many aspects of successful psychiatric rehabilitation. Because of significant impact on functional outcome, effective remediation of cognitive deficits has been increasingly cited as an essential component of comprehensive treatment. Efforts to remediate memory deficits have met with circumscribed success, leaving uncertain whether schizophrenia patients can be taught, without experimental induction, independently to employ semantic encoding or a range of other mnemonic techniques.

Method. We examined the feasibility of using memory and problem solving teaching techniques developed within educational psychology – techniques which promote intrinsic motivation and task engagement through contextualization and personalization of learning activities – to remediate memory deficits in a group of in-patients with chronic schizophrenia spectrum disorders.

Results. Although our memory remediation group significantly improved on the memory remediation task, they did not make greater gains on measures of immediate paragraph recall or list learning than the control groups.

Conclusions. Targeted remediation of memory appears to yield task specific improvement but the gains do not generalize to other memory tasks. Subjects receiving memory remediation failed to independently activate mnemonic encoding strategies learned and used successfully within training tasks to other general measures of verbal learning and memory.

INTRODUCTION

Many patients with schizophrenia have persistent and severe deficits in cognition (Gold & Harvey, 1993; Green 1998). Although the profile and relative severity of cognitive deficits in schizophrenia is markedly heterogeneous, deficits in attention, executive functioning and memory have frequently been demonstrated (Saykin *et al*. 1991; Gold *et al*. 1992; Braff 1993). While it remains unclear if memory is selectively impaired in relationship to the severity of other commonly found neurocognitive deficits (Blanchard & Neale, 1994; Hawkins *et al*. 1997), investigators have consistently shown substantial reductions in several components of verbal learning and memory (Gold *et al*. 1992; Goldberg *et al*. 1993). Procedural, implicit and long-term semantic memory are typically spared (Clare *et al*. 1993; Kern *et al*. 1997; Green, 1998); while verbal recall, recognition and working memory are often reduced compared to normal controls (Gold *et al*. 1992; Park & Holzman, 1992; Saykin *et al*. 1994; Spindler *et al*. 1997; Heinrichs & Zakzanis, 1998). Some investigators have found that deficits in recognition are relatively less severe than deficits in free recall (Koh & Peterson, 1978; Sengel & Lovallo, 1983; Calev, 1990; Beatty *et al*. 1993; Paulsen *et al*. 1995), suggesting that acquisition and retrieval deficits may be partly caused by failure to use semantic encoding automatically and other mnemonic organizational strategies (Brebion *et al*. 1997; Iddon *et al*. 1998).

Memory and other neurocognitive deficits commonly persist even after effective psychotropic treatment of psychotic symptoms

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(Medalia & Gold, 1992) and have been demonstrated to interfere with many aspects of successful psychiatric rehabilitation (Kato *et al.* 1995; Green, 1996; Penn *et al.* 1998). Verbal learning and memory deficits in particular have been shown to interfere with social skill acquisition (Mueser *et al.* 1991; Kern *et al.* 1992; Corrigan *et al.* 1994), out-patient community functioning (Jaeger & Douglas, 1992; Buchanan *et al.* 1994; Lysaker *et al.* 1995) and social problem-solving ability (Bellack *et al.* 1994; Corrigan & Toomey, 1995). Because of the significant impact on functional outcome, effective remediation of cognitive deficits has been increasingly cited as an essential component of comprehensive treatment (Storzbach & Corrigan, 1996; Kern & Green, 1998; Silverstein *et al.* 1998).

Despite growing recognition of the clinical importance of cognitive remediation and the demonstrated efficacy of remediation techniques for problem solving and attentional deficits (Bellack *et al.* 1990; Summerfelt *et al.* 1991; Goldman *et al.* 1992; Green *et al.* 1992; Metz *et al.* 1994; Kern *et al.* 1996; Stratta *et al.* 1997; Medalia *et al.* 1998), there have been relatively few studies investigating the feasibility of memory remediation. Koh *et al.* (1976) demonstrated the feasibility of modifying verbal list learning ability by experimentally inducing the use of semantic encoding strategies. More recently, O'Carroll *et al.* (1999) showed that experimental manipulation of word list learning conditions resulted in superior recall for both the schizophrenia and normal control groups, and brought the recall of the schizophrenia group up to the level of the controls. While both these studies suggest that impaired memory functioning in schizophrenia is modifiable, it remains uncertain whether schizophrenia patients can be taught without experimental induction to independently employ semantic encoding or a range of other mnemonic techniques (e.g. method of loci, peg word strategies, verbal chaining). One study has attempted to show this by examining the feasibility of remediating schizophrenia patients' memory deficits using a computer-based remediation package originally developed for use with brain-damaged patients (Burda *et al.* 1994). Captain's Log software (Sandford & Browne, 1988) was used to provide 24 half-hour sessions of cognitive training which targeted attention, memory, visuospatial skills, visuomotor skills, and conceptualization deficits in subjects diagnosed with schizophrenia or schizoaffective disorder. At post-test, 8 weeks after completion of training, the treatment group showed significant improvement on all subtests of the Wechsler Memory Scale, except for Orientation and Visual Recall. While this study demonstrates the feasibility of computer-mediated cognitive remediation of memory deficits in schizophrenia patients, it leaves unresolved the issue of specificity of treatment effects. Patients were receiving training in multiple areas of cognition so that it is unclear if memory training in isolation can be effective.

The aim of the current study was to address the issues of memory treatment feasibility and specificity, by comparing the effects of focused memory *versus* problem-solving training on the memory of schizophrenia patients. In attempting to design an effective memory remediation approach, we looked to the field of educational psychology in search of previously demonstrated effective teaching techniques. Considerable research exists in the field of educational psychology on effective teaching strategies within primary and secondary school curricula. It has been demonstrated that techniques which are able to increase intrinsic motivation, depth of engagement in the learning task, and self-perceived competence result in higher levels of learning and achievement (Lieber & Semmel, 1985; Hannafin & Peck, 1988; Lepper & Hodell, 1989; Kinzie *et al.* 1992; Bitter *et al.* 1993). Intrinsic motivation, which occurs when performance of a task is in of itself rewarding, has been shown to facilitate learning more effectively than extrinsic motivation, which occurs when a reward, for example money, is received contingent to task completion (Terrell & Rendulic, 1996). Intrinsic motivation, depth of engagement and self-perceived competence are promoted by the contextualization of learning activities in real-world or fantasy settings, by multi-sensory presentation of material, and by allowing students to personalize and control non-essential aspects of the learning environment (Cordova & Lepper, 1996). Optimization of motivation and depth of task engagement may be especially important with chronic psychiatric patients who often suffer from apathy, avolition, and poor motivation as core aspects of their illness.

Educational psychology research has informed the development of many CD-ROM based educational software programs. These programs promote intrinsic motivation and task engagement through contextualization, multisensory presentation, personalization and control. Several such programs are designed to teach effective mnemonic strategies with both verbal and visual memory tasks. These programs are typically contextualized as games or puzzle-solving exercises that simulate real life challenges. Personalized feedback and positive reinforcement are consistently presented.

We hypothesized that the same computer-based, memory-training techniques used in educational settings would also prove to be effective with schizophrenia patients. To this end, we studied the feasibility of using one of the educational software programs described above to remediate verbal learning in a schizophrenia sample. The educational program selected included several training components designed to teach a range of mnemonic encoding techniques with both verbal and visual stimuli.

With the intent of determining the specific effects of this memory remediation approach, as distinct from effects produced by training on other cognitive tasks that could potentially facilitate memory functioning, patients were randomly assigned not only to a memory remediation group and a non-treatment control group, but also to a group which participated in computer-based remediation of problem solving deficits. Problem-solving requires organization and categorization of information, skills that can potentially impact on memory. In order to determine the generalizability of changes in verbal learning, patients in the memory remediation group were assessed both for improvement within the remediation task itself and for change on other general measures of verbal learning and short-term recall. All patients were tested with these general measures before assignment to a treatment or control group, after completion of the 5-week treatment interval, and then again 4 weeks later.

METHOD

Subjects

Fifty-four in-patients at Bronx Psychiatric Center, a large, New York state-run facility for severely and persistently mentally ill persons, completed this study. A total of 560 charts from 17 different 30 bed wards were reviewed over a 2-year period. The method of sampling was non-probabilistic and purposive in nature and was done in two phases. The sampling design for chart review in phase one was based on the following inclusion criteria: (*a*) an Axis I diagnosis of schizophrenia, all subtypes, or schizoaffective disorder, using DSM-IV criteria (American Psychiatric Association, 1994), as specified in the most recent psychiatric assessment found in the medical record; and (*b*) age between 18 and 55 years old. Subjects were excluded if they were non-English speaking; had medical or neurological conditions, such as a history of head trauma, neuromuscular conditions or seizure disorder; a concurrent diagnosis of mental retardation or behavioural disturbances that required ward restrictions. Of the 560 identified patients, 141 met all study criteria and were eligible for further screening. These potential subjects were then told about the nature of the study and asked to participate in phase two screening. A subgroup of 114 patients (81% of those eligible from phase one screening), voluntarily agreed to the phase two screening which required psychological testing with the Logical Memory test and Comprehension test (described below). Patients needed to score at or below the 16%ile for normal subjects on both tests in order to establish that problem solving and memory were impaired. Eighty-seven patients completed the testing, resulting in 64 patients who met phase two screening criteria. Of those eligible for study inclusion, 60 subjects (i.e. 94% of those meeting criteria for phase one and phase two screening) signed consent and were enrolled in this study.

Recruitment into the study was continuous. Subjects were randomly assigned into one of three groups: problem solving remediation, memory remediation or control. There were 20 patients assigned to each group. Six of the 60 patients enrolled in the study dropped out of the study: two in each respective group, leaving 18 patients per group who completed the study. Reasons for dropping out of the study included withdrawal of consent, decompensation, or discharge.

All patients were being treated with a variety of medications (i.e. typical neuroleptics, atypical neuroleptics and mood stabilizers) before and during the study. Medication type and dose were independently selected and titrated on an individual basis according to the clinical judgement of the treating ward psychiatrist.

Research design

The study used a test–retest, treatment controlled design. Prior to random assignment to either of two treatment groups (memory remediation or problem solving remediation) or to the control group, all patients were pre-tested on measures of memory and problem solving. Patients in the two treatment groups then received two 25 min sessions per week for 5 weeks. The treatment control group received the standard care given at the hospital. Post-tests for all patients were performed on two occasions: (*a*) after completion of treatment (i.e. 5 to 6 weeks after initiation into the study); and (*b*) 4 weeks after the first post-test.

Procedure

Subjects and ward staff were informed that the purpose of the study was to see what helps improve 'ability to remember, concentrate and cope with tasks of daily living'. In addition to obtaining signed, informed consent, a capacity for consent was obtained from the patient's psychiatrist as per Institutional Review Board (IRB) requirements and documented in the chart. Screening evaluations were conducted individually in a quiet office. Patients were initially administered the California Verbal Learning Test, Trials 1–5, List A (CVLT–1–5), the Wechsler Memory Scale Logical Memory Test, Immediate Recall (WMS-LM-I); and the WAIS-R Comprehension Test (WAIS-R-CT). Each test was administered according to the standardized instructions. The set of instruments was counterbalanced such that order effects were controlled. Only those patients who scored at or below the 16%ile on the WMS-LM-I and WAIS-R-CT on the pre-test were considered for enrolment. In order to make this determination, one investigator (N.R.) scored all pre-tests but remained blind to group assignment until treatment was started. Subsequent post-testing on all measures was done in accordance with the timetable noted above and independently rated by a second investigator who was blind to group assignment. By so doing, rater effects were controlled, since treatment effects remained unknown until the conclusion of the study for all patients. Post-test data were available for 54 subjects for the first re-evaluation and 44 subjects for the second re-evaluation.

After initial testing, those subjects assigned to treatment conditions received either memory remediation or problem-solving remediation using intensive training through a series of micro-computerized exercises explained below. Sessions were scheduled at the rate of twice weekly for 5 weeks for a total of ten sessions. Training was provided for all subjects in both conditions by the same investigator (N.R.). All sessions took place in a quiet office on the hospital grounds with the same IBM-compatible personal computer. Those individuals who were in the control group were not exposed to the computer until after completion of the study.

Instruments

The Wechsler Memory Scale-Revised, Logical Memory test (Wechsler, 1987)

This is a brief test of verbal memory and narrative recall. The subtest devoted to Immediate Recall (LM-I) was used; the same version was administered at each testing session. The patient was read a brief paragraph that tells a story and asked to repeat it back to the examiner. Two stories are read sequentially. Inter-rater reliability is consistent because of explicit scoring criteria. The score is the units of information recalled.

The California Verbal Learning Test (Delis *et al*. 1987)

This is an individually administered assessment of strategies and processes related to learning and remembering verbal material. The Immediate Free Recall, List A, Trials 1–5 uses a standard free-recall procedure based on a hypothetical shopping list consisting of 16 items: four items each in four categories (i.e. fruits, spices and herbs, tools, clothing). Split-half reliability correlation coefficients range from 0·77 to 0·86. Score is items recalled over five trials. The same version of the test was administered at each testing session.

The WAIS-R Comprehension test (Wechsler, 1981)

This is a test of general knowledge and social problem solving. It consists of 16 questions regarding social rules and behaviours.

Treatment groups

Memory remediation

Subjects in the memory remediation group worked on a collection of activities found in 'Memory Package' (Sunburst Software; see Appendix A for product information). Five activities were selected from the package for all subjects to work on: (*a*) 'Memory Building Blocks', a matching activity using words that were revealed on a grid in order to be paired together for successful recall; (*b*) 'Simon Says', an increasing length of visual and auditory sequences that had to be recalled in the correct order; (*c*) 'What's in a Frame – Did You See This?', recall of individual items observed during an exposure to pictures for a variable time duration (e.g. 10, 20 s); (*d*) 'What's in a Frame – What Did You See?', recall of items when they were embedded in a group of items that were previously exposed for a variable time duration; and (*e*) 'Memory Castle', a list learning activity that required recall of six to 20 pieces of information in a fixed order for successful entry into the rooms of a castle. The subjects were taught mnemonic techniques (e.g. acronyms, pairing the spoken word with a visual cue) during execution of these tasks. Verbal praise and encouragement were offered in addition to tracking progress on a flow sheet for each individual patient. While each session had variability in terms of the type and number of memory activities each subject performed, the average number of minutes per activity across all subjects for all sessions were: (*a*) Memory Building Blocks = 7·8 min; (*b*) Simon Says = 4·3 min; (*c*) What's in a Frame – Did You See This = 2·9 min; (*d*) What's in a Frame – What Did You See? = 2·6 min; and (*e*) Memory Castle = 7·7 min.

Problem solving remediation

Subjects in the problem-solving remediation group worked on a software program called 'Where In the USA is Carmen Sandiego?' (Broderbund Software, Version 2·0; see Appendix A for product information). The purpose of the activity is to solve a simulated detective case by interpreting information given to identify and track the suspect in order to make an arrest. The subjects were trained to perform the sequential procedures and guided in the problem-solving process. Verbal encouragement and praise were offered to the subjects as they took risks and mastered procedures in order to perform the task. Subjects in this group typically worked on one 'case' during the 25 min session.

Control group

All subjects in the control group participated in routine unit activities (e.g. arts and crafts, medication groups) or centralized services (e.g. work-for-pay programme, leisure time) according to their unit privileges and did not receive computer remediation activities for the study period. The investigator did, however, have occasional and brief contact with control subjects on the unit when escorting peers to treatment or reminding them of appointed time for post-testing.

RESULTS

Demographics

Subjects in the two treatment groups and control group were compared on demographic variables. Descriptive statistics for these variables are presented in Table 1. The three groups were equivalent on age, SES, gender, diagnosis, and age of first hospitalization. A one-way analysis of variance (ANOVA) found a significant between group difference ($F(2,53) = 7{\cdot}23$, $P < 0{\cdot}002$) on educational level. *Post hoc* comparisons found that the mean educational level for the Memory group was significantly lower than the mean for both the control group ($P < 0{\cdot}004$) and the Problem Solving group ($P < 0.007$). The Problem Solving group did not significantly differ in educational level from the control group.

Performance on the Memory Training Task

A paired sample *t* test within the memory group demonstrated a significant change from week 1 to week 5 on a composite measure of performance on memory training tasks ($t(17) = 11{\cdot}19$, $P < 0{\cdot}001$). This composite measure was computed as the sum of correct responses for each remediation task (Memory Building Blocks, Simon Says, What's in a Frame, and Memory Castle) conducted within a training session.

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Table 1. *Demographic characteristics of* 54 *patients with chronic schizophrenia*

	Memory group (*N* = 18)	Problem solving group (*N* = 18)	Control group (*N* = 18)
Age, mean years (S.D.)	33·6 (7·7)	36·4 (6·3)	39·0 (8·0)
Education, mean years (S.D.)	9·4 (1·9)	11·4 (2·0)	11·6 (1·8)
SES (poor/working/middle)	10/7/1	6/7/5	5/9/4
Gender (male/female)	12/6	12/6	8/10
Diagnosis (schizophrenia/schizoaffective)	14/4	14/4	13/5
Age at first hospitalization (S.D.)	19 (4)	22 (4)	23 (7)

Table 2. *Pre-test and immediate post-test mean raw scores for outcome variables*

	Memory group		Problem solving group		Control group	
Variable	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test
CVLT Trials 1–5	25·7 (8·0)	29·2 (8·4)	25·6 (11·0)	27·7 (7·3)	31·3 (8·8)	34·9 (10·9)
WMS-R LM I	8·9 (3·9)	13·2 (6·0)	10·3 (4·3)	14·0 (5·2)	10·0 (4·3)	14·3 (6·8)

CVLT, California Verbal Learning Test; WMS-R LM I, Wechsler Memory Scale – Revised Logical Memory I; standard deviations are shown in parentheses.

Performance on measures of generalization

CVLT

There were no significant group differences on pre-test raw scores for the CVLT Trials 1–5. Paired samples t tests found a significant change from pre-test to immediate post-test for the control group ($t(17) = 2{\cdot}20$, $P < 0{\cdot}04$), a trend toward significant change for the Memory group ($t(17) = 2{\cdot}05$, $P < 0{\cdot}056$), and a non-significant change for the Problem Solving group (see Table 2). Paired-samples t tests from immediate post-test to the 4-week follow-up post-test found no significant changes on CVLT Trials 1–5 raw score for any of the three groups. Paired-samples t tests from pre-test to immediate post-test found no significant changes on CVLT semantic or serial clustering scores for any of the three patient groups. Repeated measures (time × group) analysis of variance (ANOVA) was used to evaluate between group differences from pre-test to immediate post-test and to 4 week follow-up post-test. No significant differences between groups were found from pre-test to either of the two post-tests (see Fig. 1). Repeated measures (time × group) analysis of covariance (ANCOVA) controlling for both educational status and atypical neuroleptic status also failed to find significant between group differences from pre-test to either of the two post-tests.

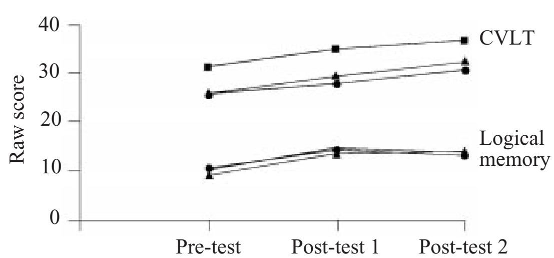

FIG. 1. Change in raw scores pre- and post-treatment. (▲, Memory group; ●, problem-solving group; and ■, control group.)

WMS-R LMI

There were no significant group differences on pre-test raw scores from the WMS-R LM I. There were significant changes from pre-test to post-test 1 for all three groups: Memory ($t(17) = 3{\cdot}30$, $P < 0{\cdot}004$); Problem Solving ($t(17) = 2{\cdot}60$, $P < 0{\cdot}02$); and control, ($t(17) = 3{\cdot}01$, $P < 0{\cdot}008$) (see Table 2). Paired-samples t tests from post-test 1 to post-test 2 (4 weeks later) found no significant changes on WMS-R LM I raw score for any of the three groups. Repeated measures (time × group) analysis of variance (ANOVA) was used to evaluate between group differences from pre-test to immediate post-test and to 4 week follow-up post-test. No significant differences between groups were found from pre-test to either of the two post-tests (see Fig. 1). Repeated measures (time × group) analysis of covariance (ANCOVA) controlling for both educational status and atypical neuroleptic status also failed to find significant between group differences from pre-test to either of the two post-tests.

DISCUSSION

Subjects receiving memory remediation significantly improved on the memory remediation task from week 1 to week 5 of training. These results provide evidence that the encoding and recall deficits often found in schizophrenia patients are malleable. Although our memory remediation group also significantly improved from pre-test to post-test on a measure of immediate paragraph recall and showed a trend toward significant improvement on a measure of word-list learning, these improvements were not significantly greater than improvements demonstrated by the study's non-treatment control group. These results suggest that our memory remediation group failed to independently activate mnemonic encoding strategies learned and used successfully within training tasks to other general measures of verbal learning and memory. Several previous studies have experimentally induced improvements in encoding and recall within training tasks (Koh *et al.* 1976; O'Carroll *et al.* 1999), but have not assessed the generalization of these improvements to other measures of learning and memory.

There are several possible explanations for why significant gains made by our memory remediation group within training tasks did not generalize to improvements on other measures of verbal recall. When comparing the current study to an investigation reported by Burda *et al.* (1994), in which cognitive remediation did generalize to significant gains on the Wechsler Memory Scale, differences in remediation group demographics are apparent. Patients included in our remediation group were younger and less educated than patients in the remediation group treated by Burda *et al.* Duration of treatment also differed between the two studies. Burda *et al.* provided 24 half-hour sessions over an 8-week period; whereas we provided 10 half-hour sessions over a 5-week period.

While different patient demographic characteristics and length of treatment are two possible explanations for discrepant results between these two studies, the most salient difference is that we offered patients very focused treatment, either of memory *or* problem solving deficits, whereas Burda *et al.* provided a comprehensive treatment of multiple areas of deficit. It may be that the additive effects of remediating attention, conceptualization, visual motor speed and memory are important for therapeutic gain. Isolated intervention of memory, or for that matter problem solving, did not result, at least in our patient groups, in a generalized improvement in memory greater than the improvement shown by our control group.

Because gains made by the remediation groups were not significantly greater than gains made by control subjects, other factors, such as practice effects, or improvement in psychiatric status across all groups, cannot be ruled out as potential causes for the memory improvement shown by all three groups. Memory impairment in schizophrenia patients has previously been associated with negative symptoms, thought disorder, severity of depression and dosage of anticholinergic medication (Levin *et al.* 1989; Tamlyn *et al.* 1992; Paulsen *et al.* 1995; Brebion *et al.* 1997). Statistically controlling for dosage of anticholinergic medication in this sample did not change our results. It remains possible, however, that the general effects of psychiatric treatment on memory may have outweighed the group-specific efficacy of our remediation, or conversely that no group improved beyond a practice effect. Field *et al.* (1997) have also found practice effects an important factor to consider when doing research on remediation.

An additional consideration involves understanding why patients failed independently to activate mnemonic encoding strategies outside of remediation tasks. Significant gains on measures of immediate recall from training week 1 to week 5 suggest that patients did learn mnemonic techniques. Failure to generalize improvements to other measures of verbal recall, as well as non-significant changes on CVLT semantic clustering scores from pre-test to post-test, suggest that, despite gains within memory remediation tasks, subjects did not independently activate newly learned encoding strategies on other measures of verbal recall. This suggests that, although the recall deficits often found in schizophrenic patients are responsive to encoding strategies, generalization of newly-trained mnemonic strategies does not occur spontaneously.

A final consideration addresses how our remediation may have failed to promote independent activation of mnemonic strategies. The computer-based remediation approach used may have increased intrinsic motivation and task engagement – which should promote learning, however, the presentation of remediation tasks was substantially different from the presentation of the outcome tests of word-list learning and paragraph recall. Possibly, other outcome measures would have been more sensitive to change. Subjects apparently did not automatically implement newly-acquired mnemonic strategies within the different context of outcome measures used. Future remediation research using computer-based training tasks may be more effective in promoting generalized use of mnemonic strategies by including teaching techniques such as faded cuing (Glisky *et al.* 1986), which have been previously demonstrated as effective in the remediation of brain-injury.

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APPENDIX A

The Memory Package is available to educators through Sunburst Communications (800-321-7511; www.sunburst.com); *Where In the USA is Carmen Sandiego*? is commercially available and can also be ordered through the publisher, Broderbund (www.broderbund.com).

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