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Approaches to Cognitive Remediation of Neuropsychological Deficits in Schizophrenia: A Review and Meta-Analysis

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A review and critique of the literature pertaining to the use of cognitive remediation techniques in patients with schizophrenia is presented. The review is organized into three sections, according to the neuropsychological deficit targeted for remediation: 1) executive-function, 2) attention, and 3) memory. With regards to executive-function, despite an initial report suggesting that Wisconsin Card Sorting Test performance cannot be remediated, subsequent studies suggest that performance can be improved on a variety of dependent measures including perseverative errors, categories achieved, and conceptual level responses. These observations were confirmed by a meta-analytic investigation that revealed large mean effects sizes ($d_+ = 0.96$) for these studies. Effect sizes were homogenous across discrepant remediation strategies and dependent measures. With regards to attention, serial scanning can be improved with instruction and reinforcement, whereas there is mixed evidence suggesting that practice-based attention drills can improve performance on measures of sustained attention in schizophrenia. With regards to memory, relatively simple semantic and affective elaborate encoding strategies elevates verbal list-learning memory in patients with schizophrenia to levels consistent with controls. A similar encoding procedure, combined with vigilance training, produces substantial improvement in social cue recognition. Avenues for future research are discussed.

KEY WORDS: schizophrenia; remediation; Wisconsin Card Sorting Test; meta-analysis.

INTRODUCTION

The purposes of this paper are (1) to critically review empirical findings regarding the use of cognitive remediation as an approach to rehabilitation of the neuropsychological deficits associated with schizophrenia; (2) based on this review, to discuss common themes and limitations across studies, and suggest fruitful avenues for further investigation. Although several articles published over the last several years have focused on the extant literature on psychosocial rehabilitation in schizophrenia (e.g., Penn and Meuser, 1996; Smith *et al.*, 1996) none of these studies has focused specifically on the remediation of neuropsychological deficits characteristic of this disorder. Two reviews published in the early 1990s (Flesher, 1990; Jaeger and Douglas, 1992) have provided overviews of the multiplicity of ways that knowledge of neuropsychological deficits in schizophrenia may inform approaches to psychiatric rehabilitation in the clinic. As much of the extant research in this area has emerged over the past 10 years, however, there was a limited empirical database to analyze at the time these reviews were written. Recently, Bellack *et al.* (1999) reviewed work on remediation, with a focus on modification of performance on the Wisconsin Card Sorting Test (WCST) in schizophrenia. The present review builds on this research by providing a quantitative meta-analysis of a subset of these studies, and including studies published since this review.

Over the past 15 years a wealth of data has accumulated regarding the presence and stability of neuropsychological impairment in schizophrenia. Most recent neuropsychological research suggests that deficits are evident in a broad range of domains including (1) verbal ability,

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(2) complex perceptual skill, (3) abstraction and cognitive flexibility, (4) attention, (5) learning, (6) sensory abilities, and (7) motor skills. Controlling for generalized deficit and medication effects, most profound decrement is evident on measures of verbal learning and memory (see Heinrichs and Zakzanis, 1998; Saykin *et al.*, 1991, 1994). Furthermore, these deficits are stable over time (Censits *et al.*, 1997) and are relatively insensitive to the effects of typical antipsychotic medication (Green, 1996). In addition, recent research suggests that although some types of atypical antipsychotic medication may produce mild improvement in the neurocognitive deficit evident in schizophrenia, significant cognitive impairment persists even after year-long treatment with these novel pharmacologic agents (Purdon *et al.*, 2000). These neuropsychological findings in schizophrenia are supported by a separate but related literature in experimental psychopathology, that has described deficits in information processing, in particular measures of attention, that are characteristic of patients with schizophrenia (see Serper and Harvey, 1994, for a review and integration of these literatures).

Surprisingly, despite these reliable findings, a relative dearth of research has investigated approaches to rehabilitation of these deficits. Several review articles have noted the lack of experimental attention to cognitive rehabilitation strategies in schizophrenia (see Green, 1993, 1996). This absence is particularly striking in light of the fact that substantial gains have been made in remediation of cognitive deficits characteristic of closed head injury (CHI; Diller and Ben-Yishay, 1987). For example, a recent study has shown that process-specific attention training for patients with CHI produced improvement on neuropsychological measures of attention relative to patients tested at identical time intervals but treated with brain-injury education classes (Sohlberg *et al.*, 2001). Few of these approaches have been applied to rehabilitation of patients with schizophrenia.

The present review will organize studies of rehabilitation according to the neuropsychological domain that they target: (1) studies of the relationship of contingent reinforcement and expanded instructions to performance on the WCST, an index of executive function. As part of this segment of the review, we conducted a meta-analysis to quantitatively assess the relative magnitude of these interventions on several dependent measures from the WCST. The uniformity of test selection, as well as the relatively large number of published reports—13, suggested that meta-analytic evaluation of this portion of the remediation literature would facilitate comparison of findings across studies. (2) Studies of the effect of attention-training procedures on performance on various neuropsychological outcome measures and (3) studies of the effect of encoding strategies for improving memory on both elementary laboratory measures and more complex measures of social cognition in schizophrenia. A final section will be devoted to an analysis of current experimental approaches to the study of rehabilitation and will offer theoretical and methodological recommendations for future research studies.

EXECUTIVE FUNCTIONS

Executive functions consist of a variety of skills including, volition, planning, concept formation, purposive action, and effective performance (e.g., Lezak, 1995). Although a variety of tests have been used to assess executive dysfunction in patients with schizophrenia, only one aspect of executive function, concept formation, has been a target for intervention. Several studies have investigated remediation of performance on the WCST, a commonly used test of concept formation and conceptual flexibility (Berg, 1948). This particular neurocognitive task has been evaluated for several reasons. First, a wealth of experimental evidence has shown stable deficits in performance on this task in patients with schizophrenia relative to healthy controls. Second, in a series of studies, Weinberger *et al.* (1986) have shown reduced indices of cerebral blood flow activation in the dorsolateral prefrontal cortex in patients with schizophrenia during impaired performance of the WCST, suggesting a possible pathophysiological basis for this deficit. Indeed, research has also revealed that nonschizophrenic siblings of patients with schizophrenia show performance deficits on measures of abstraction, including the WCST, relative to healthy controls. This finding also suggests that impairment on the WCST may represent genetically-linked, hard-wired neural impairment (Cannon *et al.*, 1994). Third, according to some investigators, remediation of impaired performance may speak to the underlying source of this impairment. By this view, if impaired performance is related to a core cognitive deficit in rule-learning or concept formation, presumably dependent upon prefrontal neural circuits, there would most likely be limited ability to teach patients to perform well on this task. Fourth, and probably most importantly, problem-solving deficits are clearly a core aspect of the behavioral symptomatology of schizophrenia. Any remediation of these deficits could potentially produce marked changes in social and occupational functioning.

A growing body of literature suggests that, with proper instruction, performance on the WCST can be improved in schizophrenia. However, considerable debate exists regarding the nature of instruction necessary to remediate performance as well as how easily the skills necessary for completion of this task generalize to other tasks that require similar problem-solving skills.

Early attempts at remediation of WCST deficits failed to produce significant results. Goldberg *et al.* (1987) in a study of 44 inpatients (mean age was 31 and 32 years for the two experimental groups) with schizophrenia investigated the effects of informing subjects about the nature of the categories, the occurrence of shifting sets and card-by-card instructions on percent correct, percent perseverative errors, and the number of categories achieved. Only under conditions of card-by-card instructions were significant improvements evident on the three dependent measures. Furthermore, the results were short-lived, no evidence of improved performance was observed either immediately or 2-weeks after initial training. The authors concluded that impaired WCST performance in schizophrenia was a stable deficit reflecting impaired prefrontal neural circuits rather than nonspecific psychological factors. Notably, the sample was markedly impaired and was selected as those chronically hospitalized patients who were least likely to do well on this task, and thus may not be representative of the schizophrenia population at-large.

Clearly, Goldberg's findings do not completely rule out the possibility that the persistent deficits in WCST performance observed in their patients is related to limited motivation or other psychological factors. To address this issue, Summerfelt *et al.* (1991) investigated the effect of positive reward on performance on the WCST in patients with schizophrenia. Fourteen patients were assigned to a crossover design in which the WCST was administered twice in counterbalanced order, once with standard instructions alone and once with monetary reinforcement and standard instructions. An initial stake of $7.50 was placed in a bowl in front of the subject prior to test administration in the monetary reinforcement condition. Monetary reward consisted of a 10-cent gain for each correct response and a 5-cent cost for each incorrect response. The results revealed significant increases in percent correct responses, smaller percent perseverative errors, and greater total earnings for patients in the monetary reward condition relative to the standard verbal feedback group on trial one. Notably, total number of categories achieved was not significantly different between the two groups. The authors concluded that perseverative errors in card sorting performance most likely reflect motivational, as well as cognitive difficulties.

Several investigators have attempted to integrate the Weinberger and Summerfelt findings. Bellack *et al.* (1990) examined both the issue of instruction and reinforcement in an experiment in which hospitalized patients (mean age = 32.4 years) were assigned to one of two cohorts: Subjects in cohort one received contingent or noncontingent reinforcement during performance on the WCST. Reinforcement consisted of 5 cents administered after every correct response for the contingent reinforcement group. In the noncontingent group subjects received 5 cents on every trial the contingent group received 5 cents, regardless of whether the response was right or wrong. In cohort two participants were administered contingent reinforcement along with expanded instructions on the WCST. Expanded instructions included detailed explanations of the principles by which patients can sort cards as well as an explanation of the conditions under which the sorting rule can change. Instructions were expanded and modified in an interactive approach that was contingent on patient understanding. Performance for both cohorts was measured before, during, and 1 day after training. The results showed that contingent and noncontingent reinforcement failed to produce any change in task performance as measured by number of categories correctly sorted, percent correct response, or percent perseverative responses. Thus poor performance on this task does not appear to be dependent exclusively upon a lack of motivation or attention. In cohort two, expanded instruction along with monetary reinforcement had a marked impact on performance. A significant effect of training was evident upon all three dependent measures in this group, including, most importantly, number of categories achieved. This latter finding suggests that remediation in this study did not simply reflect learning not to make the same wrong response consecutively, a critique raised of other studies that focus solely on perseverative errors as an outcome measure (Goldberg and Weinberger, 1994). The enhancement was stable over a 1-day period. Limitations of the study included the limited time frame sampled after training and the failure to assess generalization of training to related problem-solving measures.

In a similar study, Green *et al.* (1992) showed significant increases in number correct, perseverative errors and number of categories completed when subjects were given specific incremental trial-by-trial instructions (similar to those of the Goldberg study) along with monetary reinforcement. Additional experimental conditions investigated the use of monetary reinforcement alone in enhancing performance. Consistent with the findings of Bellack *et al.* (1990) monetary reinforcement alone had no effect on overall WCST performance suggesting that deficits were not purely related to a lack of motivation. The study, however, also did not examine the consistency of these effects over time.

Young and Freyslinger (1995) investigated WCST performance in 41 chronically hospitalized patients (mean age = 41.3 years; mean education = 11.3 years), divided into one of two experimental groups. The first group received card-by-card or "didactic" training, similar to that of Weinberger and Bellack. A second experimental group received flexible, “scaffolded” instruction in which patients’ performance was observed and the researchers made a determination of what components of the task were not understood. Depending upon this determination, different patients might be taught different skills. For example, one patient might be taught the concept of matching, whereas a second patient, with different impairments, might be taught the significance of verbal feedback in relation to previous card placement. In this way, training was tailored to each individual patient’s impairment.

The results revealed a significant increase in the number of categories completed, and an increased percent conceptual learning along with a decrease in percent perseverative errors for the “scaffolded” group. The “didactic” group showed a nonsignificant effect of instruction on categories achieved but significant effects on percent conceptual learning and percent perseverative errors. Notably, performance was enhanced after instruction for both groups four weeks after original training. Performance on a related but different problem-solving test (the Short Category Test) was also enhanced at a level that approached statistical significance. Thus, there is some evidence that problem-solving skills acquired on the WCST may generalize to a related task.

The failure to find a significant increase in number of categories completed in the “didactic” condition is somewhat unexpected in light of previous findings reported by Bellack. There are two likely sources for the discrepant results. First, there is a marked difference in sample composition between these studies. In the Bellack studies, subjects were disqualified only if their performance exceeded five categories completed during baseline WCST testing. At baseline subjects completed roughly one-and-a-half categories. Contrastingly, Young and Freyslinger only selected patients who completed less than three categories successfully at baseline. Their subjects could only sort to a mean of 0.43 categories before intervention. Thus, the Young and Freyslinger sample was restricted to a limited subset of patients who were unusually impaired on this task. Second, Young and Freyslinger examined the impact of didactic training alone, without increased levels of motivation produced by monetary reward.

Recent studies have replicated Bellack’s findings and provided strong evidence that changes in performance are durable over a 4–6 week period. Metz *et al.* (1994) investigated the effects of incremental instruction in an approach similar to that of Bellack *et al.* in patients with schizophrenia, affective disorder, and schizoaffective disorder. Consistent with previous findings there was a significant improvement in categories achieved, percent perseverative errors, and percent conceptual level responses for patients with schizophrenia. These effects persisted in an attenuated form over an average of a 6-week delay for percent conceptual responses and percent perseverative responses. The durability of improvement in number of categories achieved was not reported. Strengths of this study include the long length of delay between training and test, comparison of results between schizophrenia patients and other psychiatric patients, and replication of the training procedures of Bellack and Weinberger. In a related study employing Bellack’s training procedures, Nisbet *et al.* (1996) found that chronically hospitalized patients with schizophrenia improved their performance in terms of error responses, categories completed, perseverative responses, and perseverative errors on the WCST. This improvement was maintained up to 24 hr after training, without any type of monetary reinforcement.

Two other studies have yielded strong support that deficits on the WCST can be remediated by a variety of intervention strategies. Stratta *et al.* (1994) in a study of 20 patients with schizophrenia (mean age = 34.8 years; mean education = 9.7 years) investigated the effect of forcing patients to verbally express the criterion for matching before card sorting. Patients were not instructed as to how to complete the task. The authors found a marked improvement in the number of categories successfully sorted after verbal criterion expression in a subset of 8 out of 13 patients who showed impaired performance on this task. Notably, there was only a minimal effect on total perseverative responses and total errors. The improvement in number of categories successfully sorted however was short-lived and was not evident when patients were tested the following day.

Using a very different approach to remediation, Kern *et al.* (1996) in a study of 11 chronically ill inpatients (mean age = 33.2 years; mean education = 11.2 years) investigated the effect of errorless learning training on number of categories achieved, perseverative errors, and percent conceptual level responses on the WCST. Errorless learning training, adapted from animal studies of errorless discrimination training, consists of analyzing the WCST into component parts, ordered according to difficulty level. In this study, step-wise training began with the simplest components of the WCST (e.g., stimulus feature identification), in which there was a high probability of correct responding. Training then was applied to incrementally harder tasks (e.g., shifting sorting principles). Difficulty was increased minutely, so high levels of performance were maintained across all steps. The results revealed improved performance on all three dependent measures, relative to a pretreatment baseline, that was maintained even 4 weeks after training. After treatment, performance was indistinguishable from patients who did not have deficits in WCST performance.

Recent research has provided the most persuasive evidence that instruction, not reinforcement, is crucial for improved performance on the WCST. In a study of 32 inpatients with schizophrenia, Hellman *et al.* (1998) investigated the effects of monetary reinforcement (high vs. low) and instructions (present vs. absent) on number of categories completed, number of correct responses, and number of perseverative errors on the WCST. The results indicated significantly improved performance on all three dependent measures in the incremental instruction group. Paradoxically, high levels of reinforcement produced a trend toward poorer performance on perseverative errors and number correct. There was no evidence, on any of the dependent measures, that higher levels of reinforcement improved WCST performance. The authors concluded that deficits in WCST performance are not related to deficits in motivation but instead reflect enduring neurocognitive impairment that is sensitive to remediation strategies. In contrast to previously reviewed studies, improved performance on the WCST did not persist over a 1-week delay.

In order to better assess the magnitude of the effect of rehabilitation interventions on WCST performance, we performed a meta-analysis of the studies reviewed in this section. Articles reviewed in this section and included in the meta-analysis were identified through a computer-based PsychInfo (American Psychological Association, 2000) search conducted from the beginning of this database (1887) to the present. The search was conducted using the following key words: schizophrenia, WCST, remediation. A parallel search using the same key terms was completed with the MEDLINE (National Library of Medicine, 1994) database from 1966 to the present. The reference sections of articles located from both searches were studied for relevant citations.

Analyses were conducted according to procedures suggested by Rosenthal (1986) and Hedges and Olkin (1985). The dependent measures included the following WCST indices: (1) categories attained (CAT), (2) perseverative errors (PER), and (3) conceptual learning (CLR) expressed in Cohen's *d* (Cohen, 1977; Glass, 1977). The *d* score is the difference between intervention type (i.e., treatment versus control) or pre–post intervention conditions (i.e., baseline versus follow-up), within each study or comparison, expressed in standard deviation units. Study statistics were converted to *d* using formulas provided by Glass (1977). Of the 13 studies available for review, three studies did not present data that allowed for the calculation of an effect size and were subsequently excluded from analysis (Goldberg *et al.*, 1987; Green *et al.*, 1992; Stratta *et al.*, 1994). When studies included several posttraining assessments we selected the initial assessment after training. For seven studies the posttraining assessment occurred immediately after training on the same day. For the remaining studies the assessment was the next day after training. With the exception of one study, training occurred in a single day. By expressing effect size in standard deviation units, we were able to make a direct comparison of outcomes across studies.

Each analysis was conducted in several steps. First, Hedges *g* was derived for each study using *t*, *F*, or *p* statistics reported in the individual study (Hedges and Olkin, 1985; Rosenthal, 1994). Although Hedges *g* is an estimate of effect size, the *g*-statistic is known to overestimate the population effect size when sample sizes are small (Rosenthal, 1994). In order to correct for this bias, Hedges *g* was subsequently transformed into an unbiased measure of effect size, Cohen's *d* (Hedges, 1981; Hedges and Olkin, 1985). Individual values of *d* were thereafter combined across studies and weighted according to their variance. Potential differences in effect size between studies were analyzed using the method of Hedges and Olkin (1985). This procedure computes mean weighted effect sizes and 95% confidence intervals (CI) for each variable subset and allows for the testing of the influence of each individual factor on the overall results. For further discussion and details concerning meta-analytic techniques, the reader is referred to the works of Cooper and Hedges (1994), Hedges and Olkin (1985), Hunter *et al.* (1982), and Rosenthal (1986).

Table I shows the mean weighted effect sizes (d_+) for schizophrenia patients on CAT, PER, and CLR from the WCST following structured intervention procedures. The composite effect sizes for intervention on the WCST across all three dependent variables (CAT, PER, and CLR) would be considered "large" in that most were at or above what Cohen (1977) characterized as a large effect (≥ 0.80). Specifically, results of homogeneity analysis indicated that across the three WCST variables examined, the effects of rehabilitation techniques on performance were generally quite robust ($d_+ = 0.98$, 95% CI $= 0.80/1.16$). This effect was consistent across studies, $Q(20) = 17.6$; $p = .61$, suggesting that any variations in the intervention applied, or WCST variable examined, did not influence the magnitude or consistency of the effect. In order to further detail the magnitude of the effect size for each individual WCST variable, we conducted a categorical contrast between CAT, PER, and CLR (see Table II). Consistent with the overall analysis, no significant differences were seen between WCST variable types, $Q_B(2) = 0.79$; $p = .68$, or within CAT, PER, or CLR. Notably, the effect sizes for each variable type were quite large, suggesting a

Table I. Remediation of Wisconsin Card Sorting Test (WCST) Performance in Schizophrenia

Author	Type of intervention	Number of subjects[a]	Chronicity[b]	WCST variable	Effect size (Cohen's d)
Bellack *et al.*, 1990	Expanded instructions, rehearsal, feedback, and contingent reinforcement	28 inpatients	Acute	CAT	1.27
				PER	0.22
Summerfelt *et al.*, 1991	Contingent reinforcement	4 inpatients 10 outpatients	Acute & Chronic	PER	0.79
Goldman *et al.*, 1992	Expanded instructions	24 inpatients	Acute	CAT	0.92
				PER	1.43
Metz *et al.*, 1994	Expanded instructions	19 inpatients	?	PER	0.62
				CLR	0.92
Young and Freyslinger, 1995	Expanded instructions	14 inpatients and outpatients	Chronic	CAT	0.62
				CLR	0.58
Young and Freyslinger, 1995	"Scaffolded" instruction	14 inpatients and outpatients	Chronic	CAT	1.09
				CLR	1.36
Vollema *et al.*, 1995	Expanded instructions, rehearsal, and feedback	22 inpatients and outpatients	?	CAT	1.78
				PER	1.49
Bellack *et al.*, 1996	Expanded instructions, rehearsal, and feedback	9 inpatients	Acute	CAT	0.94
Kern *et al.*, 1996	Errorless learning	11 inpatients	Chronic	CAT	0.64
				PER	0.80
				CLR	0.79
Nisbet *et al.*, 1996	Expanded instructions	10 inpatients	Chronic	CAT	1.25
				PER	1.18
Hellman *et al.*, 1998	Expanded instructions vs. Contingent reinforcement	16 inpatients	Chronic	CAT	1.44
				PER	1.44

Note. CAT: "categories attained"; PER: "perseverative errors"; CLR: "conceptual learning."
[a]Number of subjects used for computation of effect size.
[b]"Acute" refers to those patients that were trained and tested while hospitalized for an exacerbation of symptoms; "Chronic" refers to those patients that have had more than one psychotic episode but were not necessarily experiencing an exacerbation of symptoms at the time of study.

generalized effect of intervention on WCST performance. One caveat regarding these findings, however, is that this meta-analysis combined effect sizes across studies that included subjects of varying clinical status, some in acute symptom exacerbation, others more stable. Thus, because of the effect of clinical state on neuropsychological test findings, some variance was introduced into the effect size analysis not attributable to the intervention.

In summary, studies of remediation of WCST performance have revealed that (1) deficits are not solely attributable to deficits in attention or motivation or both; (2) that while a variety of approaches to instructional remediation have been employed, we can say with some degree of confidence that explaining the task with an interactive approach, regardless of the specific content of instruction, yields a fairly substantial effect. Notably, the effects of intervention are quite large in the short term, regardless of the specific WCST performance index studied; (3) there is some evidence that remediated performance can persist, at least in an attenuated form, over a 6-week period; and (4) asking the patient to verbalize the rule they are using to sort will improve some aspects of performance for a brief period of time (less than 24 hr). A prominent limitation of these studies is that, in all cases, researchers have evaluated the effects of remediation with the same instruments that they use to train participants. Recent research has addressed this important limitation, and has revealed that extended cognitive flexibility training, without specific experience on the WCST, produces mild improvement on the WCST in patients with schizophrenia (Wykes *et al.*, 1999). A second, related limitation is that evidence of generalization of remediation-linked improvement on the WCST to other nontrained measures of executive-function clearly does not necessarily address the functional significance of improved performance. To provide an ultimate test of

Table II. Tests of Categorical Model for Intervention Effects on Three WCST Indices

Class	k	d_+	95% CI	Q_w
Categories	9	1.08	0.80/1.37	5.80
Perseverative errors	8	0.93	0.64/1.21	9.10
Conceptual learning	4	0.90	0.52/1.28	1.95

Note. $Q_B = 0.79$, $p = .68$; Class: WCST variable type; k: number of studies in analysis; d_+: mean weighted effect size; 95% CI: 95% confidence interval for d_+; Q_w: within-class effect; Q_B: between-class effect.

the generalization of these remediation procedures, future studies will need to assess the relationship of improved WCST performance to more ecologically-valid measures of executive-function that map more closely onto activities of everyday living. A third limitation is that although it is clear from the preceding studies that improvement on the WCST cannot be attributed to monetary reinforcement alone, improved performance may still represent increased motivation secondary to interaction with an experimentor. Thus, these interventions may treat both deficits in abstraction and apathy. Future studies that include control groups to test for the nonspecific effects of clinician interaction will be crucial for dissociating the relative role of these factors.

ATTENTION

Early studies of attention function in the area of experimental psychopathology were motivated by theoretical interest in Broadbent's "bottleneck" theory of attention processes in which the human mind is viewed as a limited-capacity processing channel or filter (Broadbent, 1958). In these studies, impaired reaction time, span of apprehension, and other elementary aspects of attention were interpreted as deficits in the patients attention filter or channel capacity (see McGhie and Chapman, 1962). Since this time, a large body of research has evaluated attention processes in schizophrenia. Although considerable theoretical and empirical progress has been achieved, until recently, few studies have investigated approaches to remediation of deficits in attention. The studies conducted thus far have yielded mixed results.

In one of the earliest studies of rehabilitation of attention in schizophrenia, Wagner (1968) investigated the effects of contingent reinforcement and repeated practice on a variety of neuropsychological outcome measures: the Similarities subtest of the Wechsler Adult Intelligence Scale (WAIS), Proverbs Test, Memory for Designs Test, Letter Circle Test, and the Peabody Picture Vocabulary Test. These tests were administered at a pretraining baseline and after 4 days of training with a delayed-matching-to sample test. Performance in remediated subjects improved on four out of the five tasks relative to contact and no-contact control groups. Strengths of the study included carefully selected control groups that addressed the effects of exposure to the experimenter, contact with the training apparatus, and noncontingent reinforcement. Additional strengths were counterbalanced training procedures and a variety of neuropsychological outcome measures. Limitations included (1) limited assessment of the durability of remediation over time, (2) use of a delayed matching-to-sample task, a task typically used to assess memory, as a training task for attention, and (3) small sample size ($n = 8$).

In another early study, Meichenbaum and Cameron (1973) investigated the effects of a self-instructional (SI) training procedure in altering the attention, thinking, and language behaviors of hospitalized schizophrenia patients. In Experiment 1 subjects were taught to (a) verbalize the nature and demands of the task, (b) practice cognitive rehearsal and planning to help maintain task focus, (c) give self-instructions in the form of self guidance, (d) give coping self-statement to handle failure and frustration, and (e) provide self-reinforcement to maintain task perseverance. The results showed significant improvements in performance on a digit-recall and a digit-symbol task relative to control groups who received either no-treatment or met with the experimenters and practiced tests but did not receive specific SI training. In Experiment 2, an expanded SI training procedure was used to include covert rehearsal for social interactions. A wider range of dependent variables was assessed. Results indicated that SI training (1) produced stronger digit-recall performance under conditions of distraction; (2) produced more abstract interpretations of proverbs in patients, and (3) reduced number of irrelevant verbalizations to interview questions. Strengths of these experiments included the practice and nonpractice control groups and the range of dependent measures that were evaluated. Limitations included the high level of effort required to teach such highly sophisticated cognitive training techniques. The authors concluded that this process of instruction produced substantive gains in elementary cognitive functioning as well as enhanced performance of more complex psychosocial task performance.

A plethora of studies have demonstrated slowed reaction time to a target stimulus in schizophrenic patients (see Neuchterlein, 1977). Healthy controls benefit on a reaction time task when a target stimulus is presented with consistent, rather than variable, interstimulus intervals. Patients with schizophrenia however show *slower* performance on regular intervals relative to irregular intervals of a reaction-time task. This phenomenon has been labeled the redundancy-associated deficit and is of particular interest as it is a trait-marker of schizophrenia that is present during both acute psychotic episodes and during periods of disease remission. Steffy and Galbraith (1980) investigated the effect of encouragement and monetary reward on overall reaction time and the redundancy-associated reaction time deficit in 16 schizophrenia inpatients. These training procedures produced stable decreases in overall reaction time that were comparable to performance levels of healthy controls. In contrast, despite the extensive training procedures, patient's performance still showed evidence of the redundancy associated deficit. The authors concluded that (1) overall reaction time and the redundancy associated deficit are independent, (2) overall reaction time can be modified by positive reinforcement in schizophrenia patients, and (3) the redundancy deficit is a more enduring and elementary deficit in cognition in schizophrenia, and is less sensitive to behavioral modification.

In a related study, Benedict and Harris (1989) evaluated the effect of attention, memory, and concept formation software training programs on reaction time in 20 patients (mean age = 30.3 years) with schizophrenia hospitalized for over a year. The results revealed that 25 training sessions with the software produced decreases in reaction time, relative to an attention-placebo and no-treatment control group. A strength of this study was the inclusion of the attention-placebo control group, where subjects met with an experimenter, completed the same computer training tasks that experimental subjects did, but their were no advancement criteria as subjects completed the tasks in a prearranged order. Thus, training effects could not be attributed to exposure to the software program per se, or to nonspecific reinforcing effects of meeting with an experimenter every week. The effects of this training on other cognitive functions, higher level social-occupational functioning or even other aspects of attention, however is unclear. A limitation of this study was the small sample size ($n = 5$).

Benedict *et al.* (1994) investigated the effects of six attention-training tasks selected from a large pool of commercial software for brain-injured adults, on the degraded stimulus Continuous Performance Test (CPT), the Span of Apprehension Test (SAT), and the Word List Recall Task (WLRT). These tasks were selected in light of previous research showing that impaired performance on these tasks reflects a durable, trait-related deficits rather than transitory state measure of schizophrenia. Thirty-eight chronic patients (mean age = 37.9 years; mean education = 11.9 years) were randomly selected from an outpatient day treatment center and were administered the six training tasks over a total of 14–15 sessions conducted twice per week. Training tasks were selected for their requirement of sustained vigilance and high degree of mental effort. One exercise required the patient to respond as quickly as possible whenever they saw a yellow square on the computer screen, and to inhibit responding when they saw a blue square. Feedback was given on reaction time and accuracy. A second exercise required the subject to simultaneously monitor several lines of colored moving squares on a screen at the same time, and to respond to a square of a target color whenever it passed through the center of the computer screen. Other exercises included visuomotor tracking and serial addition tasks (Bracey, 1982). The CPT, SAT, and WLRT were administered before and after training. Results *failed* to show a significant effect of training on all but one of the dependent measures. The authors concluded that there was little evidence from this study to suggest that practice of controlled cognitive processing enhances performance on measures of attention. The authors recommended that more attention be paid to rehabilitation strategies that compensate for, rather than remediate, neuropsychological deficit.

In a study of rehabilitation of more elementary attention mechanisms somewhat different conclusions were reached. Kern *et al.* (1995) investigated the effects of enhanced instructions and monetary reinforcement on performance on the Span of Apprehension Test (SAT). This test is designed to assess the number of items that can be attended to at one time. The span has typically been measured by having subjects identify selected target stimuli or entire stimulus arrays immediately following their presentation. This measure has been of particular interest as deficits on this task represent a trait marker of schizophrenia, present both during and after symptom exacerbation (see Neuchterlein and Dawson, 1984). Subjects were administered a series of individual test trials and were instructed to identify which of two target letters (T or F) appeared on a screen. Letter arrays were presented for brief durations and the location of the target letter was randomly distributed among 16 possible target locations. The investigators showed that in 40 inpatients (mean age = 35.2 years; mean education = 11.7 years), percent correct on this serial scanning task increased in participants given both contingent monetary reinforcement and enhanced instruction and was consistent with that of healthy controls. Contingent reinforcement or enhanced instruction did not produce as large an effect when presented alone. Furthermore, a follow-up indicated that this remediation was relatively stable over a 1-week period. The authors concluded that simple attention mechanisms can be remediated through enhanced instruction and reward. Strengths of this study included careful comparison of motivational vs. cognitive factors in remediating attention performance.

The finding that attention deficits in schizophrenia can be remediated, has been replicated in a second study involving a different approach to rehabilitation, and a different measure of attention. In a study of 54 inpatients (mean age = 32.5 years; mean education = 10.8 years), Medalia *et al.* (1998) evaluated the effect of a 6-week, 18-session, computerized attention remediation program on performance on the Continuous Performance Test (CPT). The attention remediation program had previously been used with head injury patients. The results showed significant improvement in the treated group, relative to an untreated control group, on CPT right letter detection, wrong letter detection, and absolute percent correct. Interestingly, there was also significant improvement in symptoms, as measured by scores from the Brief Psychiatric Rating Scale (BPRS), in remediation-treated subjects. The authors concluded that practice and behavioral learning remediates core attention deficits in schizophrenia, at least to a modest degree. Strengths of this study included a large sample size, assessment of symptoms as well as neurocognition, and careful control procedures. Limitations included a failure to evaluate the stability of this improved attention performance after training.

A summary of the articles reviewed in this section is presented in Table III. In conclusion, studies of remediation of deficits in elementary aspects of attention have yielded mixed results. Clearly, flexible, domain-specific, self-instructional programs appear to be effective in helping reduce attention deficits as measured by digit span and psychomotor speed, along with a variety of other behavioral measures in schizophrenia. These programs, however, are highly effort-intensive. Serial scanning processes can be improved with a combination of reward and careful instruction. The repetitive practice of controlled cognitive processing characteristic of many brain-injury rehabilitation training programs, has produced mixed benefit in schizophrenia. It is a strength of this research domain that the majority of the foregoing studies reviewed in this section evaluated the effects of remediation on tasks that were distinct from those used for remediation training. Further research is necessary to (1) specify with greater precision the conditions under which repetitive attention practice will or will not aid attention function in schizophrenia; (2) investigate whether positive effects on measures of simple attention will generalize to measures of other aspects of attention, and (3) assess the durability of remediated attention over time.

MEMORY

In recent years, an increasing amount of research has investigated memory deficits in schizophrenia. Studies have documented greater impairments in verbal memory than in other cognitive functions and these deficits do not appear to be accounted for by abstraction or attention (see Gold *et al.*, 1992; Saykin *et al.*, 1994). One explanation for these deficits is that patients encode semantic information poorly. Several studies have shown that patients group or "cluster" semantically related words on a list learning tasks at a lower rate than that of controls (see Koh *et al.*, 1973; Paulson *et al.*, 1995). Other research has revealed that patients show less proactive interference than controls, again suggesting reduced semantic encoding (see Kareken *et al.*, 1996).

Healthy subjects, when asked to study a list of words that differ in degree of "pleasantness" typically remember significantly more "pleasant" than "unpleasant words" when asked to subsequently recall that list, a phenomenon that has been described as the "Pollyanna" effect. Contrastingly, patients with schizophrenia, when asked to study and recall the same word list perform significantly more poorly and do not show the "Pollyanna" effect, i.e., they remember unpleasant, neutral, and pleasant words at equally low rates. This result has commonly been attributed to blunted affect or "anhedonia" in patients with schizophrenia. In an interesting series of experiments, Koh

Table III. Rehabilitation of Attention Deficits in Schizophrenia

Author	Intervention	Sample size (*n*)	Chronicity	Results
Wagner, 1968	Practice on attention tasks	8	Chronic	Significant improvement in Memory for Designs Test, Proverbs, Similarities subtest of the WAIS-R, and Peabody Picture Vocabulary
Meichenbaum and Cameron, 1973	SI training procedure	5	Mixed	Significant improvement on digit-symbol subtest of the WAIS-R and an auditory distraction task
Steffy and Galbaith, 1989	Monetary reward and verbal encouragement	16	Chronic	Improved simple RT; no effect on redundancy associated deficit
Benedict and Harris, 1989	Computerized attention exercises	16, 17	Chronic	Improved simple RT
Benedict *et al.*, 1994	Computerized attention exercises	16, 17	Chronic	No improvement on the CPT or the SAT
Kern *et al.*, 1995	Monetary reward and enhanced instructions	10	Chronic	Improved span of apprehension test
Medalia *et al.*, 1998	Orientation Remediation Module (ORM)	27	?	Significant improvement on right and wrong letter detection on the CPT and BPRS total score

Note. CPT: Continuous Performance Test; RT: Reaction Time; SAT: Span of Apprehension Test; BPRS: Brief Psychiatric Rating Scale.

et al. (1976) have evaluated the effects of manipulating semantic and affective processing of words on this recall deficit evident in subjects with schizophrenia. In these studies, hospitalized patients with schizophrenia, hospitalized nonschizophrenic psychiatric patients, and healthy controls were instructed to study a 50-word list by writing down and then rating each word on a 7-point pleasantness–unpleasantness scale. The results showed that schizophrenic patients performed at a level consistent with psychiatric patients and normal controls both on initial and subsequent free and cued recall tasks. Thus, forcing schizophrenic patients to elaborate encoding processing on both affective and semantic dimensions remediates the deficits evident on these types of verbal list-learning tasks.

Corrigan *et al.* (1995) investigated a combined program of vigilance and memory training on social cue perception in schizophrenia. Forty-six patients (mean age = 35.3 years; mean education = 12.6 years) were randomly assigned to a vigilance alone or vigilance-plus-memory training condition. The stimulus materials for both training conditions were eight videotaped vignettes from the Social Cue Recognition Test. This test consisted of two or three actors who acted-out scenes that are rated by subjects as low or high in emotional content. Vigilance training comprised a self-instruction procedure similar to that of Meichenbaum, using salient cues and repeated practices. In the vigilance plus memory condition, subjects were asked to use the strategy of semantic elaboration employed by Koh *et al.*, for remediating verbal memory deficits in schizophrenia. Subjects in the vigilance-plus-memory enhancement condition were better able to recognize social cues presented in taped vignettes than subjects participating in the vigilance alone control condition, even 48 hr after training. The results of this study are of particular importance for several reasons. First, they compared two methods of cognitive remediation directly, to begin to evaluate the active "ingredient" in various rehabilitation programs. Second, they related remediation of basic neuropsychological deficits to a much more complex psychosocial activity, i.e., social cue perception. Third, they evaluated the persistence of their findings 48 hr after training. A limitation was the failure to report pretreatment baseline scores.

In summary, whereas many studies have documented memory deficits in schizophrenia, relatively few studies have investigated remediation of these deficits, even as compared with the number of reports that have investigated executive-function and attention training. Initial studies provide reason for optimism. Relatively simple semantic and affective elaborate encoding strategies elevated verbal list-learning memory in patients with schizophrenia to levels consistent with controls. A similar encoding procedure, combined with vigilance training, produced substantial improvement in social cue recognition. Further studies are needed to address the stability of these improvements over longer periods of time, and to investigate the effectiveness of these encoding strategies on different to-be-remembered stimulus materials.

CONCLUSIONS AND AVENUES FOR FUTURE RESEARCH

Although not exhaustive, the current review suggests that there are several common characteristics of studies that have evaluated the effects of remediation of neuropsychological deficits in schizophrenia. *One* clear finding is that a broad range of neuropsychological functions have been targeted for remediation. However, future research should target those areas of neuropsychological deficit that are particularly responsible for the profound social dysfunction evident in schizophrenia. Different neuropsychological deficits may not contribute to social dysfunction equally. Fortunately, there has been increasing attention to the relationship between specific neuropsychological dysfunction and community outcome, social problem solving and social skills acquisition over the past several years (see Green, 1996, for a review). The findings from these studies should help guide us as we design more refined approaches to remediation.

A *second* finding is that, despite clearly divergent research strategies for remediation of performance on the WCST, effect size estimates for different studies were large and homogenous. This suggests that the wide array of approaches to remediation produce similarly profound effects on performance on the WCST. The ecological significance of these findings is still unclear. Research has revealed a relationship between performance on the WCST and several measures of occupational function (Lysaker *et al.*, 1995). In fact, one study that prospectively evaluated the relationship of perseverative errors on the WCST to vocational functioning in a mixed sample of psychiatric patients revealed that patients with poor vocational outcome made nearly three times as many perseverative errors as those with good outcomes (Jaeger *et al.*, 1993). Clearly, performance on the WCST is linked to poor psychosocial status in psychiatric samples. Nonetheless, the impact of improved performance on the WCST, as described in the foregoing studies, on the pronounced psychosocial deficit evident in schizophrenia, is still uncertain.

A *third* finding is that no researchers, to our knowledge, have specifically evaluated the effects of individual differences on sensitivity to remediation procedures. Many of the studies reviewed in this paper did not report sample characteristics beyond basic demographic data. This absence is particularly noteworthy in a neuropsychiatric disorder as heterogeneous as schizophrenia. Patients differ widely in premorbid cognitive abilities, duration of illness, symptoms and pattern of neuropsychological deficit, and these characteristics may have implications for therapeutic benefit. Results from future remediation studies, in which patients are stratified according to differences in these characteristics, will help guide the appropriate utilization of health care resources by identifying those patients who will benefit most from specific approaches to remediation.

A related issue is the degree to which patients should be screened for significant neurocognitive impairment prior to treatment with these remediation procedures. It is possible that only a subsample of patients with specific neurocognitive deficit may benefit from these procedures. Recent research suggests that as many as 27% of patients with schizophrenia in some samples are neuropsychologically "normal" (Palmer *et al.*, 1997). Although the majority of the WCST studies reviewed in this first section of this paper screened patients and only treated those with significant deficits on this task, other studies in this review have not screened subjects on this basis. Thus, effects of remediation may be obscured in these studies by baseline "ceiling" level performance.

A *fourth* finding is that the relation of other treatment approaches, most importantly pharmacologic intervention, to cognitive remediation has not been elucidated. Some recent research suggests that atypical antipsychotic medications, such as Risperidone, Olanzapine, and Clozapine may influence neurocognitive function in the absence of remediation (Meltzer and McGurk, 1999). All of the studies described in this review trained and tested patients who were stabilized on neuroleptic medication. Thus, observed improvement in these studies reflected an interaction between medication and behavioral treatment. Few remediation studies to date have reported the type of medication patients were treated with during training procedures. Thus, the extent to which different antipsychotic medication may maximize benefit from remediation programs is unclear. Future research should evaluate the effects of cognitive remediation in patients stratified according to treatment with atypical or typical neuroleptics.

A related issue is the relationship of neurocognitive remediation to other behavioral treatments in schizophrenia such as psychosocial skills training (Liberman *et al.*, 1989). Reducing the impact of rate-limiting cognitive deficit in schizophrenia could have profound consequences for acquisition of social skills.

A *fifth* finding is that nearly all investigators in this research domain have utilized the standard experimental approach in which group statistics are evaluated to determine the probability that observed effects between experimental and control groups could have occurred by chance. Although this method has clearly yielded many interesting findings, it is somewhat surprising that parallel efforts have not been directed toward single-case research designs. The single-case design is appropriate for changes in cognition that occur over time, particularly for such a heterogeneous disorder as schizophrenia. Single-case design allows (1) analysis of differences in treatment responses that may offer clues to remediation of neuropsychological deficits in patients that present with widely differing levels of symptomatology and cognitive impairment; (2) monitoring that individual subjects are motivated and attentive during training and testing; and (3) yielding robust and interpretable data with a relatively small number of subjects, in a research area where lengthy, effort-intensive behavioral intervention protocols can make large patient samples prohibitive.

The case study approach, in conjunction with group studies, has yielded important insights regarding impairments in supervisory attention systems in schizophrenic patients (see Shallice *et al.*, 1991). The single-case design also has been employed effectively to assess the effect of lengthy attention and memory attention training programs for head-injured patients (see Sohlberg and Mateer, 1987). Although simple A-B designs are subject to a variety of potential confounds, more sophisticated multiple baseline designs allow for inference regarding the source of treatment effects as opposed to spontaneous recovery or nonspecific therapeutic effect (see Barlow and Hersen, 1984). Positive results from single-case studies can serve as a basis for group studies with relatively homogenous subject populations.

In conclusion, from the current set of studies reviewed it is clear that some measures of executive function, attention, and memory can be remediated with extra-instructions, repeated practice, or reinforcement or both. Future studies should be aimed at (1) assessing how neuropsychological deficit may be remediated most efficiently, e.g., proper length of treatment and the active ingredients of current remediation approaches; (2) the durability of remediated neuropsychological test performance over months and years; and (3) the degree to which remediation of performance on specific neuropsychological tasks generalizes to other tasks and to more complex psychosocial functions. This last issue emerged and continually reemerged in this literature review and is of the utmost importance. If patients are unable to incorporate the effects of neurocognitive remediation into their behavioral repertoire, and transfer remediated neuropsychological skills across settings, the potential therapeutic gain of these rehabilitation procedures is clearly of limited scope. This important issue has been directly addressed in a study by Bellack *et al.* (1996). In that study, patients were either trained on the WCST or the modified Vygotsky Concept Formation Task (VCFT) and were subsequently tested on both tasks. These tasks were selected as similar measures of concept formation and set shifting. The results revealed that patients who showed remediated performance on the WCST did not show improved performance on the second concept formation task (the VCFT). Clearly, further research is needed to address the generalizability of this finding and to assess whether other remediation strategies may generalize more easily across different settings and to different tasks.

As is clear from the current review, great advances have been made in the description and analysis of elementary deficits in information processing in schizophrenia. Initial attempts at cognitive remediation have appropriately targeted these elementary deficits for remediation. Future research should be aimed at integrating remediation of several aspects of executive function, attention, and memory as part of a comprehensive protocol for cognitive rehabilitation. Furthermore, it is abundantly clear from the current review that most studies have examined relatively chronic patients, with some being hospitalized long-term (see Tables I and III). The increased literature documenting that cognitive deficits are present at first presentation and in unaffected siblings (e.g., Cannon *et al.*, 1994) suggests that some are "hard-wired" and related to brain capacity. This has implications in two domains: prevention for people at risk and early intervention, maximizing pharmacologic and neurocognitive approaches with educational programs.

Finally, the integration of this type of research with direct measures of brain anatomy and physiology can help elucidate the pathophysiology of the disorder and neural processes mediating these deficits and their amelioration. For example, with respect to the WCST remediation studies, it is unclear whether improved performance on this task reflects activation of previously quiescent dorsolateral prefrontal brain regions, or alternatively whether improved performance reflects the acquisition of new functions by brain regions that were intact prior to training. The implications of the duration of treatment effects for brain physiology are also unclear. Future functional imaging studies will play a crucial role in elucidating the central mechanisms for both improvement on neuropsychological tasks and the maintenance of that improvement over time.

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