Abstract

Increasing awareness of the importance of neurocognitive impairments in schizophrenia has fostered considerable interest in the prospects for cognitive rehabilitation. Nevertheless, optimism has outpaced progress. We first review recent literature on the central assumptions that underlie cognitive rehabilitation, including the hypothesis that cognitive deficits play a central role in social disability and other problems schizophrenia patients experience in daily living, and that these impairments must be rectified if we are to achieve effective rehabilitation. We next discuss developments in knowledge about the neurobiology of schizophrenia that bear on the potential for cognitive rehabilitation and the selection of appropriate targets for intervention. Third, we propose a new research strategy for investigating cognitive functioning in schizophrenia and for examining the relationship of cognitive deficits to role functioning in the community: examining patients who have good vocational outcomes in order to identify strengths or compensatory factors that compensate for core deficits. We present new data that lend support to our proposed approach. We next discuss putative limits to cognitive rehabilitation based on data documenting cognitive deficits in healthy siblings and parents. Finally, we briefly describe an interim rehabilitation strategy that minimizes the load on cognitive processes rather than attempting to improve cognitive functioning.

Key words: Rehabilitation, neuropsychology.


This special issue of the Bulletin is an exciting and timely update on a persistent topic in the literature on schizophrenia over the past decade: cognitive rehabilitation. The history of interest in this topic dates back at least as far as Meichenbaum’s seminal work in the early 1970s (Meichenbaum and Cameron 1973). With a pair of provocative studies, he generated considerable interest in the possibility of teaching patients to use self-talk to guide problem solving. Platt and Spivack (1972a, 1972b) provided some thought-provoking data on problem solving during that period that also pointed to a role for cognitive rehabilitation. These somewhat anomalous studies were not replicated, however, and interest in cognitive training languished as the emphasis of psychosocial treatment shifted to more promising interventions that were more consistent with the increasingly sophisticated neurobiological models of schizophrenia: namely, behavioral skills training and family psychoeducation. Frustration continued with the failure of these techniques and available medications to substantially enhance daily functioning in the community. It was certainly possible to reduce psychotic symptomatology, family conflict, and relapse and rehospitalization, as well as to improve social skills, but patients continued to suffer from poor role functioning. It was also becoming increasingly apparent that schizophrenia was marked by significant cognitive impairments that were not ameliorated by psychopharmacological interventions (Spohn and Strauss 1989).

Two studies in the late 1980s rekindled dormant interest in cognitive rehabilitation: Brenner and his colleagues (1990) described Integrated Psychological Therapy (IPT), a comprehensive program to improve social competence by first enhancing basic cognitive skills, and Goldberg and colleagues (1987) reported that patients with schizophrenia were unable to benefit from explicit instructions and practice on the Wisconsin Card Sorting Test (WCST), a putative neuropsychological marker of prefrontal function. This failure to benefit from training, combined with data on diminished blood flow, was interpreted as evidence of an unmodifiable abnormality of the dorsolateral prefrontal cortex. The first of these reports held out the promise for effective cognitive reha-
bilitation, while the second implied that a basic neurophysiological impairment made such rehabilitation impossible. The field quickly mobilized to either replicate and expand upon the innovative work of the Swiss group or to refute the pessimistic conclusions of the National Institutes of Health (NIH) group. The NIH work stimulated a spate of mostly successful demonstrations that WCST performance deficits, albeit widespread, are neither endemic to the illness nor immutable; we will discuss some of that literature below. The Brenner project stimulated a lively, thought-provoking debate in a previous special issue of the Bulletin in 1992 (vol. 18, no. 1). As will also be discussed below, Brenner’s results were not particularly robust and have not yet evolved into a more effective iteration. Nevertheless, that work has had tremendous heuristic value and still serves as the most systematic test of the feasibility of cognitive rehabilitation to date.

One of us (A.S.B.) contributed a paper to the 1992 special issue entitled, “Cognitive Rehabilitation for Schizophrenia: Is It Possible? Is It Necessary?” (Bellack 1992). As might be inferred from the title, we were not particularly sanguine about the prospects for either Brenner’s program or then-current thinking about cognitive rehabilitation, notwithstanding our view that Goldberg et al.’s (1987) even more pessimistic conclusion was not empirically justified. Our intention in this article is to revisit the issues addressed in 1992 in light of subsequent research and to propose new directions for the field. First, we review the basic arguments made in the earlier article and discuss relevant findings from the intervening years that bear on the conclusions. Second, we discuss developments in understanding of the neurobiology of schizophrenia that bear on the potential for cognitive rehabilitation and the selection of appropriate targets for intervention. Third, we will propose a new research strategy for investigating cognitive functioning in schizophrenia and for examining the relationship of cognitive deficits to role functioning in the community. We will then present some new data that lend support to our proposed approach. Finally, we will briefly describe an interim rehabilitation strategy that minimizes the load on cognitive processes rather than attempting to improve cognitive functioning.

**Pertinent Issues in 1992**

Bellack’s 1992 article identified three assumptions that appeared to be common to much of the work on cognitive rehabilitation: “(1) Cognitive impairments play a central role in the social disability and other problems schizophrenia patients experience in daily living. (2) These impairments must be rectified if we are to achieve effective rehabilitation. (3) The prognosis for cognitive rehabilitation, as reflected in preliminary studies, is quite positive” (Bellack 1992, p. 44). Each of these assumptions was judged to be conjectural and preliminary at best.

**The Role of Cognitive Impairments in Social Disability and Problems in Daily Living.** In discussing the first assumption, we agreed in 1992 that there was strong evidence for the existence of substantial cognitive impairments in schizophrenia, but indicated that there was scant evidence to demonstrate which, if any, specific deficits accounted for a significant proportion of the variance in functional behavior in the community or which should be the targets of rehabilitation efforts. Much of the rehabilitation literature focuses on social competence, a domain that is critical for effective role functioning in the community and in which schizophrenia patients have well-documented deficits (Bellack et al. 1990a). As summarized in a seminal paper by Michael Green (1996), a number of studies in the intervening years have documented a relationship between diverse measures of neuropsychological capacity and both social functioning and performance in skills training programs. There appears to be a replicable association between analogue measures of social competence and measures of verbal memory and attention (Green 1996). For example, we found relationships between verbal memory and social problem solving, social skill, and response to social skills training (Mueser et al. 1991; Bellack et al. 1994). We are currently conducting a study on substance abuse in people with schizophrenia that replicates our previous findings on the relationship between social skill and verbal memory. Correlations were calculated between scores on our problem-solving battery (Sayers et al. 1995) and IQ (based on the vocabulary and information scales on the Wechsler Adult Intelligence Scale–Revised [WAIS-R]) and the Wechsler Memory Scale–Revised (logical memory I, digits forward, and digits backward). Role-play performance on our battery was significantly correlated with IQ ($r^{27} = 0.34, p < 0.04$) and with logical memory ($r^{27} = 0.40, p < 0.02$). Role-play skill was not correlated with digit span, and none of the correlations between the cognitive measures and the problem-solving component of our battery were significant.

Similar results have been reported by Green and colleagues (Kern et al. 1992; Bowen et al. 1994; Corrigan et al. 1994), who found significant relationships between measures of verbal memory and visual information processing and measures of social skill. While the effect sizes in these small sample studies have been modest, there is a fair degree of consistency across studies in terms of which specific cognitive measures correlate with which specific
measures of social skill. Two important limitations to these data relate to the analogue nature of the measures of social skill. Social competence in each of these studies was assessed with some form of simulated social interaction, rather than by observing patients in the community. For example, our studies are based on the Social Problem Solving Assessment Battery, in which subjects engage in a series of simulated 3-minute conversations with a staff member portraying someone from the outside environment (e.g., a parent, a landlord). The interactions are videotaped and subsequently rated on a variety of specific verbal and nonverbal response attributes (e.g., speech fluency, ability to negotiate). There is extensive empirical support for this approach to rating social skill (Bellack et al. 1990). Analogue measures are robust markers of social skills in the person’s response repertoire. But social performance in the community depends on a number of factors in addition to having the capacity to perform a behavior in controlled circumstances, such as motivation to engage in social interaction and prior experience in similar encounters. It would be very tenuous to conclude that modest correlations between neurocognitive measures and analogue measures of social skill document a meaningful relationship between neuropsychological deficits and functional behavior in the community. Few data directly support the thesis that the replicable deficits in information processing have an impact “downstream” and substantially account for the deficits in community functioning in general, or social functioning in particular (Benedict et al. 1994). We present preliminary data below to suggest that neuropsychological deficits may play a significant role in the capacity to work, but that the contribution of neuropsychological functioning may differ in patient groups with good versus poor vocational outcome. Nevertheless, the widely held assumption that neuropsychological deficits have important functional consequences has not been adequately investigated.

A second factor that limits conclusions about the relationship between social and neuropsychological functioning is shared “method variance.” Several of the studies in this area have used measures of social skill and social skill learning that place heavy demands on memory and attention. For example, the Bowen et al. (1994), Corrigan et al. (1994), and Kern et al. (1992) studies assessed acquisition of medication management skills on an assessment battery that required subjects to listen to an examiner read two paragraphs about the topic and then answer a series of questions about the material, answer additional questions after watching videotapes about medication management, and then demonstrate a series of specific steps that had been illustrated on another videotape. These tasks require subjects to pay close attention to the videotaped presentations and then recall the material. Not surprisingly, both studies found significant correlations between performance on these measures and verbal memory (Rey Auditory Verbal Learning Test) and vigilance (Continuous Performance Test and Digit Span distractibility), tests that require substantially the same cognitive operations.

The hypothesis that social performance and skill learning depend, at least in part, on verbal memory and vigilance has considerable face validity. It seems implausible that someone could effectively negotiate a rapidly unfolding social encounter without being able to carefully monitor the partner’s behavior and remember what has been communicated earlier in the conversation. Reduction in working memory capacity, which appears endemic to schizophrenia (Gold et al. 1997), would also place limits on an individual’s ability to engage in negotiation, social problem solving, and other complex conversational processes. However, it is still unclear how much variance each of these cognitive processes accounts for, or (as discussed below, in the context of good vocational outcome patients) the extent to which some people with the illness may learn to compensate for the deficits.

Another example of the effects of method variance comes from the literature on social perception deficits. A number of studies have reported that people with schizophrenia have difficulty correctly labeling affect depicted in photographs of faces or in brief videotapes of social interactions (Morrison et al. 1988; Bellack et al. 1992; Cramer et al. 1992; Heimberg et al. 1992; Kerr and Neale 1993). Based on this literature, it was assumed that schizophrenia is marked by focal deficits in social perception (especially the perception of negative affect) and that this deficit should be a critical target for cognitive rehabilitation efforts. For example, social perception training is an important component of Brenner’s IPT.

The assessment methods employed in many of the studies finding perception deficits placed a premium on attention as well as affect perception per se, and/or only assessed perception on a narrow range of situational content. In response, we conducted a study that examined the parameters of social perception more extensively (Bellack et al. 1996). The primary measure of affect perception was a videotape that was empirically developed for this study. It consisted of 30 brief (mean = 15 second) videotaped segments of conversations abstracted from movies and television shows. The test was first administered without sound and then readministered 30 minutes later with the soundtrack to determine if performance was improved when the additional information, provided by the auditory cues, was available.

Contrary to expectations, schizophrenia (and schizoaffective) patients did not exhibit a consistent, specific deficit in the ability to perceive affect. A subsequent
reexamination of the literature indicated that support for
the hypothesis that there is a focal deficit in affect percep-
tion is actually quite tenuous. Most studies that found per-
ception deficits used very brief stimuli, thereby placing
high attentional demands on subjects, or tested highly
impaired chronic patients whose motivation and attention-
capacity was suspect. With the exception of a study by
Heimberg et al. (1992), studies that included nonaffect
perception control tasks found that schizophrenia patients
have a generalized performance deficit rather than a spe-
cific deficit in affect perception. Overall, the data indicate
that, with the possible exception of highly impaired
chronic patients, schizophrenia patients can make accu-
rate judgments about affect when they are given adequate
time and information (Gessler et al. 1989; Joseph et al.

These findings on social perception are consistent
with another concern raised in our 1992 article: Decisions
about which aspect of information processing to target
were premature. More extensive information is now avail-
able about the nature of cognitive deficits in schizophre-
nia. Nevertheless, the most appropriate targets for rehabili-
tation remain unclear. Liberman and Green (1992) and
Spring and Ravdin (1992) both addressed this issue in dis-
cussing appropriate “levels” of intervention. Liberman
and Green, for example, wondered whether Brenner’s
focus on problem solving initiated training too far “down-
stream from the source of the problem” (p. 30). The criti-
cal question in selecting neurocognitive targets is one of
generalizability: How far reaching are the effects of train-
ing on any basic information-processing domain? This
issue is not unique to schizophrenia, but has been the sub-
ject of extensive research on thinking and skill and the
acquisition of cognitive skills in nonimpaired populations
as well. The problem is encapsulated in a recent review by
Ericsson and Hastie (1994): “Consistent with human
information processing theory, the attainment of skill and
expertise appears to entail only the acquisition of domain-
specific knowledge and pattern-action connections with-
out changing basic processes and information-processing
capacity limits” (p. 48). They go on to state that, “contrary
to expectations, the search for measures of basic capacity
that correlate with performance in complex tasks of
everyday life have been mostly unsuccessful” (Ericsson
and Hastie 1994, p. 55). If more than 30 years of research
on normal populations has failed to identify a critical role
for modification of basic processes, serious questions
must be raised about the prospects for people with schizophre-
nia. The point here is not that basic processes do not
serve as critical building blocks for complex, functional
behaviors and skills, but rather that their contribution to
highly skilled and highly routinized behavior may not be
linear or additive.

Cognitive Impairments Must Be Rectified If We Are to
Achieve Effective Rehabilitation. The status of this
second assumption is more tenuous than the status of the
previous assumption about the relationship between neu-
ropsychological and social/role functioning. As indicated,
a number of studies have reported robust relationships
between skill acquisition in training programs and verbal
memory and vigilance. The studies by Green and col-
leagues are limited by method variance, while our studies
were based on brief trials with either acutely ill (Mueser
et al. 1991) or highly chronic patients (Mueser et al.
1995a). Despite the specific limitations, the cumulative
impact of these studies does provide convergent support
for the thesis that amelioration of cognitive deficits could
be helpful. Conversely, there is no support for the con-
tention that cognitive remediation is essential. This
assumption of necessary remediation is consistent with
the restorative model that has long dominated treatment
of mental illness, including schizophrenia. This restora-
tive model assumes that impairments can and should be
corrected in order to achieve an effective rehabilitation
outcome. Failure to eliminate the underlying impairment
is thought to be akin to palliative attempts to reduce fever
and headache, rather than eliminating a viral infection.
While this model is quite viable in the realm of infectious
disease and orthopedics (e.g., repair of broken bones), it
has not proven to be useful for mental health. There is lit-
tle evidence that either psychopharmacological or psy-
chosocial interventions have been effective in eliminating
any disorder, let alone schizophrenia and its sequelae.
The compensatory model common to many areas of reha-
bilitation medicine is much more appropriate. The
emphasis is not on eliminating impairment so much as
minimizing the resultant disability. Individuals who are
blind or have paraplegia are taught to use prosthetics for
mobilization and to adjust physical aspects of their envi-
ronment to facilitate performance of activities of daily
living (ADLs) as well as recreational and occupational
activities. A parallel strategy for people with schizophre-
nia would entail reducing demands on verbal memory
and vigilance, rather than reducing impairments in these
domains. For example, extensive evidence suggests that
over-learned skills become automatic, thereby reducing
the load on working memory (Ericsson and Hastie 1994).
Improving working memory may be necessary to enable
patients to deal with novel situations, but the skills
needed for many ADLs and daily tasks and demands can
be anticipated. Over-learning of key skills and compen-
satory strategies could be sufficient to enhance compe-
tence in these routinized activities. Similarly, the role of
attention and working memory in learning may be mini-
mized by modifying the format and content of training.
We provide an example of such a program below.
The Prognosis for Cognitive Rehabilitation Is Quite Positive. The third assumption in 1992 was that optimism about the potential for cognitive rehabilitation was justified. Disputing this optimistic forecast essentially entails the fruitless task of proving the null hypothesis that cognitive rehabilitation is not possible. However, we can determine the level of optimism that is justified today by examining the accumulating evidence in two domains: the efficacy of interventions developed to date and the nature and basis of the cognitive impairments in the disorder.

Much of the work on cognitive rehabilitation in the past 6 years has focused on the WCST, a measure of complex problem solving and "executive" capacity that is a putative marker of metabolic activity in the dorsolateral prefrontal cortex. The initial Goldberg et al. (1987) publication concluded that schizophrenia patients have tremendous difficulty improving their WCST performance despite explicit instruction. In contrast, a series of subsequent studies has shown that deficits exhibited by schizophrenia patients on the WCST are not immutable. In an initial study, we demonstrated that a brief cognitive-behavioral intervention could produce significant improvement in WCST performance that was maintained at least until the following day (Bellack et al. 1990c). Similar to other variations in the literature (see below), our technique involved an iterative teaching paradigm in which information about the test was explained in small units, after which subjects were required to express the same information in their own words. Once they understood the task, correct performance was modeled and subjects were required to demonstrate their ability to respond correctly. Incorrect responses were followed by corrective feedback and additional practice. They were also required to verbalize their strategy after the first few correct responses; corrective feedback was given if the reasoning was faulty even when the card placement was correct.

We recently replicated this finding in the context of a multi-site collaborative trial of clozapine. The study was conducted at the University of California at Los Angeles (Steven Marder), University of Pittsburgh (Nina Schooller), and Hillside Hospital (John Kane). Schizophrenia patients were recruited for a comparative trial of clozapine and haloperidol. They were assessed on a large battery of measures, including the WCST, at baseline and at the conclusion of a 24-week double-blind medication trial. After completing the followup assessment, subjects received the WCST training protocol employed in our prior study. The procedure was manualized to facilitate dissemination across the three sites, and all sessions were videotaped to ensure fidelity. The WCST was readministered in standard fashion the day after training, and these data were used to evaluate the effects of training and the contribution of clozapine to training effects. Subjects exhibited marked deficits in WCST performance at the baseline assessment, and there were virtually no pre–post changes in the clozapine condition on any WCST variable (or treatment-by-time interactions) despite marked improvements in psychopathology. Conversely, our WCST training protocol was highly effective in improving WCST performance for clozapine patients, and there was no differential learning benefit. Seventy-seven percent of subjects increased the number of correct responses from pre- to post-training, with the mean increase being 23.09 percent; 65.38 percent of subjects exhibited a decrease in the number of perseverative errors, with a mean decline of 16.57 percent. In addition, neither pre- to post-treatment changes on the WCST nor performance in the WCST training protocol was correlated with symptomatology (Brief Psychiatric Rating Scale and Scale for the Assessment of Negative Symptoms). In addition to replicating our previous findings on the training protocol, these data also highlight the importance of individual differences in both baseline performance and response to training (e.g., 23% of subjects failed to improve on number of correct responses, and 34.62% failed to decrease perseverative errors). We discuss this variability at greater length below.

Other laboratories have been able to produce comparable effects using our training strategy (Vollema et al. 1994; Nisbet et al. 1996) and slightly different variations, with improvements lasting from several weeks (Kern et al. 1992; Metz et al. 1994) to 1 month (Young and Freyslinger 1995). These data document that training can produce robust changes in WCST performance. The interventions were not designed to produce a meaningful change in general problem-solving style or capacity (i.e., on tasks other than the WCST), however. The findings would have limited heuristic or clinical value if they illustrate only that patients can be taught a circumscribed rule that clarifies the somewhat anomalous WCST procedure. In fact, some support for the latter possibility is provided by several studies in which appropriate instructions, without training per se, were shown to be sufficient to produce significant improvements in WCST scores (Goldman et al. 1992; Stratta et al. 1994). These findings suggest that at least some patients may perform poorly primarily because they are confused by the vague instructions. While inability to comprehend the instructions might itself reflect some impairment, it is not consistent with hypotheses about focal (e.g., frontal) impairments in problem solving or ability to maintain set. Alternatively, either the simple instructions or the brief training may circumvent the need for subjects to generate a model for solving the task, thus vitiating the purpose of the test, which is to evaluate the subject’s ability to develop and sustain focus on a model. In either case, these data do not verify any
substantive change in information-processing style or capacity.

Two recent studies have attempted to explicate the significance of these training analogues by examining the generalizability of training effects across problem-solving tasks that require comparable cognitive operations but that present different types of stimuli and operate according to different rules. We conducted a pilot study in which subjects were first tested on the WCST and the Vygotsky Category Test (Wang 1987), a problem-solving task in which subjects sort three-dimensional wooden blocks. They were then trained on one of the two instruments, and then retested on both. The WCST training was highly effective, but we were unable to demonstrate cross-test generalization with our small sample as the Vygotsky test proved to be comparatively easy and all groups exhibited some pre–post improvement. In contrast, Young and Freyslenger (1995) recently reported that improvement in a WCST training protocol was associated with better performance on the Halstead Category Test. Their small sample study did not include a baseline measure of category test performance, so it is not certain that subjects improved after being trained on the WCST (i.e., generalized); better performers on the category test may simply have been more able to benefit from WCST training. This important issue should be examined further in larger scale trials employing appropriate controls for practice effects.

In a handful of published studies, cognitive training strategies have been employed to improve performance on other measures of information processing. Benedict et al. (1994) employed a computer-based training program that had been developed to enhance attention in brain-injured patients. While subjects improved their performance on the computerized tasks, there was no associated improvement on Asarnow and Nuechterlein’s Span of Apprehension Test or degraded stimulus Continuous Performance Test (CPT). Consistent with our position stated above, the authors concluded that compensatory approaches were more advisable than attentional retraining until more powerful cognitive intervention strategies were developed. Burda et al. (1994) employed a different computer-driven cognitive retraining protocol and reported pre- to posttraining improvements on the overall score from the Wechsler Memory Scale and the Trailmaking Test (both Trails A and B). These data are somewhat difficult to interpret as their VA sample did not exhibit the expected cognitive deficits at baseline. In a recent study by Wexler et al. (1997), subjects were given extensive practice on a motor dexterity task and either a visual reading task or a dot spatial memory task. Improved performance was gradually shaped over 10 weeks. A majority of subjects reached normative levels on the reading and dot tasks, and most showed improvement on the dexterity task as well. These results are consistent with other studies (e.g., Goldman et al. 1992; Stratta et al. 1994) that demonstrate that modest improvements can be observed on a variety of tasks with practice alone or practice supplemented by incentives.

One possible explanation for this effect is suggested in an innovative study by Schmand et al. (1994). They demonstrated that performance on putative “trait” markers of schizophrenia (including measures of vigilance, verbal memory, and distractibility) was related to independent measures of motivation on cognitive tasks, and that performance on the motivation measure could be enhanced with accurate feedback. These findings do not indicate that replicated findings on the existence of cognitive deficits are artifacts, but rather that transient practice-based improvements can result from enhanced effort and motivation. People with schizophrenia can, apparently, mobilize resources to perform better in special circumstances, whether by compensatory strategies or as a result of decreased demand on processing capacity. This hypothesis was supported in a recent study by Kern et al. (1995) in which simple instructions and monetary reinforcement were sufficient to increase performance on a measure of span of apprehension, a putative trait marker of schizophrenia that is thought to be highly stable. These findings should temper overly optimistic interpretations of data on analogue studies of rehabilitation techniques. The accumulated findings provide clear evidence that performance can be enhanced on a range of cognitive tasks through practice, instruction, and provision of incentives. Thus, the extent of impairment observed on initial formal testing may not provide an accurate assessment of potential competence. However, these practice-related changes typically fall short of full normalization of performance and may not be long lived. Such results do suggest that the deficits present on formal testing likely represent a combination of stable as well as more plastic factors (e.g., demoralization and lack of motivation). However, the more important issue remains that the gains achieved in these studies do not appear to have had large clinical effects on other aspects of functioning. If it were that easy to produce meaningful change, industrious clinicians or creative researchers would have solved the problem long ago!

These analogue studies can shed considerable light on the potential for changing information-processing style or capacity, but they do not resolve questions about the impact of any such changes on community functioning. Unfortunately, there has been a dearth of new data on clinical applications of cognitive rehabilitation strategies. Brenner and his colleagues have conducted several small sample studies on IPT (Brenner et al. 1994). This sophisticated, multi-layered program was “state of the art” when
first described at scientific meetings in the late 1980s, and it remains the most ambitious effort to date. The program has considerable face validity and has had great heuristic value. However, the results have been modest at best. There have been improvements on several of the neuropsychological tasks targeted in training, akin to the practice effects reported in several of the analogue studies referred to above. However, there has not been evidence of widespread improvements in cognitive functioning or generalization to higher level domains (e.g., social skill).

Spaulding and colleagues (Spaulding et al. 1997; 1999, this issue) have translated the Brenner materials into English and have been engaged in a replication trial at a long-term hospital for chronic patients in Nebraska. The preliminary results appear to be no better than the results of the Brenner trial. Modest improvements were made on a few tests from a comprehensive neuropsychological assessment, but these results could have been due to chance, given the number of statistical tests conducted. In discussing the prior literature, Spaulding et al. (1999, this issue) conclude, “the improvements observed in previous studies may not be any different from changes in normal subjects who practice an unfamiliar task, and there are no previous indications that such changes confer ecologically significant benefits in personal or social functioning” (p. 280). Spaulding et al. are more sanguine about the implications of their own recent findings. While we agree with their interpretation of the previous literature, their preliminary reports do not lead us to share their optimism about their program.

Judging the potential for cognitive rehabilitation based on existing trials (analogue or clinical) is difficult due to the risk of Type II error. It may be safe to conclude that a particular strategy is not effective, but one cannot extrapolate from any single trial or group of trials to the broader domain. For example, a particular technique that fails to produce an effect in 10 training sessions might be effective after 50. Ten sessions of practice on computerized memory tasks may not be sufficient to produce a generalizable increase in processing capacity, but meaningful changes might begin to occur after 100 sessions. Alternatively, an innovative program based on a different conceptual model could produce results that the simpler practice/rehearsal strategies currently in vogue do not. Nevertheless, the current literature does not provide strong grounds for optimism.

Selection of Targets for Rehabilitation

For the most part, the targets for rehabilitation have been selected based on replicated evidence of deficits compared with nonpatient controls. Essentially, it has been assumed that if patients do worse than controls on some capacity X, improving performance in X would result in improvements in some important dimension of role functioning. This approach has two potential drawbacks: (1) the remediable deficits may not account for much variance in role functioning, in which case even effective rehabilitation would have little functional impact, and (2) some early onset deficits or phenotypic characteristics may not be remediable.

We propose a different approach to the selection of rehabilitation “targets”: the study of “expert” performance, an approach common in cognitive psychology (Sternberg 1994). The study of unusually competent subjects sharpens the focus to the traits and abilities associated with success, as opposed to the correlational literature examining schizophrenia outcome, which has been most revealing of deficits linked to failure. Clearly, our use of the term expert is somewhat loose. However, this framework has several advantages. First, there is broad agreement that outcome in schizophrenia is multidimensional, with only modest correlation across the symptomatic, social, and vocational domains (Strauss and Carpenter 1972, 1977; Carpenter and Strauss 1991). The contrast of patients who demonstrate unusually good outcomes in each of these different domains or other dimensions of interest (e.g., ability to live independently) to those with poorer functioning is the most direct method of examining the specific determinants of each outcome dimension. In addition, in the cognitive literature, the study of expertise emphasizes that the cognitive functions involved in “novice” versus expert performance often differ (Ericsson and Hastie 1994). For example, chess masters plan their tactics many moves further ahead than novices, and they can scan a chess board much more quickly to evaluate options. They do not necessarily have greater reasoning skills or visual memory than novices; rather they have so much experience in game situations that they have developed a large knowledge store of characteristic game sequences and patterns that they access in a relatively automatic, non-attention-demanding fashion. In fact, they are no better than novices at remembering the configuration of pieces placed on the board randomly rather than in prototypical game configurations.

Some people with schizophrenia may have impairments (e.g., in working memory or visual scanning) that make it impossible to advance beyond the novice (i.e., impaired) level; however, some deficits may not actually be critical for higher level performance. Continuing with the chess analogy, some patients may be able to become highly familiar with typical game configurations (an applied skill), thereby enabling them to become better at predicting the opponent’s next move (a cognitive skill).
without any fundamental improvement in their general problem solving or reasoning capacity: They may simply have learned that X frequently follows Y. This skill might correspond to a vocational situation in which a patient learns to efficiently deliver packages to a series of specific addresses but is unable to plan a daily route or determine what to do if a recipient is not there to take delivery. The patient could be an expert in following a predetermined route plan, but a novice in developing a delivery schedule. Training that focuses on the latter might be fruitless if the person has deficits in sustained attention or working memory that make it impossible to deal with multiple variables at once.

In our view, studying the characteristics of good outcome or "expert" patients may reveal the skills needed to succeed in the face of schizophrenia. A parallel approach would be to compare patients with their well siblings who share vulnerability indicators but are able to function well in the community. Such skills are clearly logical targets for rehabilitation, and it remains an empirical question whether this training will prove possible to achieve levels of expert or simply more competent performance in the more typical patient with schizophrenia who presents with multiple cognitive and social deficits.

We (J.G. and R.W.B.) have adopted this hypothesis in addressing vocational functioning in patient samples drawn from the Maryland Psychiatric Research Center (MPRC). Several relatively recent North American follow-up studies have documented that a small minority of patients with schizophrenia are able to hold competitive employment, with variation across studies likely explained by differing sample characteristics and rating criteria (Harding et al. 1987; McGlashan 1988; Breier et al. 1991; Harrow et al., in press). Results from the Chestnut Lodge study, Chicago followup study, and a survey of the current patient census at the Outpatient Research Program of the MPRC all suggest that 10 percent to 20 percent of patients demonstrate a relatively good vocational outcome. The actual employment of these patients often appears to be at a lower level than might be expected on the basis of familial demographic features. However, in our view, any successful competitive employment is an important achievement for a patient with schizophrenia and demonstrates that the diagnosis of the illness is not fully synonymous with functional disability.

To examine the relationship of cognitive measures and outcome, we examined archival data from the Outpatient Research Program at MPRC and classified patients as having a good or poor vocational outcome (GVO and PVO, respectively). Patients were classified as GVO if they had two or more ratings of 4 on the Strauss-Carpenter Level of Functioning Scale (Strauss and Carpenter 1972) work item, indicating they had at least 1 year of full-time work while in treatment at the MPRC. Any patient who had only one rating done while at the MPRC and received a rating of 4 on that occasion was also classified as GVO (a single rating covers a 6-month period). The cognitive performance of the GVO group was contrasted with all other schizophrenia patients (here considered PVO). Thus, this is a conservative approach, including in the PVO group some patients who might be considered to have at least a moderately good vocational outcome because they may have had some part-time work.

The Outpatient Research Program at MPRC is an outpatient clinic where patients receive their primary psychiatric care and participate in a variety of neuroimaging and neuropsychological studies. To be admitted into the clinic, patients must meet diagnostic criteria for schizophrenia (established using a best-estimate approach combining structured interview data, medical records, and family informants when available) and be free of serious medical or neurological illness that would complicate their research participation, including substance dependence. Length of participation varies widely, ranging from patients who come to the clinic to participate in a specific clinical trial to those who have received their care at the MPRC for 10 or more years. The majority of patients maintain involvement with the clinic for a number of years, allowing for the clinical-research staff to develop a clear, detailed picture of the longitudinal course of their illness.

The sample on which we present data below did not differ significantly in age (GVO = 35.9 [standard deviation 6.7], PVO = 36.0 [8.1]), gender (male GVO = 70%, male PVO = 65%), or race (33% and 36% African American in GVO and PVO, respectively). There were significant differences in education (GVO = 13.8 years [2.3], PVO = 11.9 [2.1]; t = 4.02, p < 0.01) and age at onset (GVO = 24.6 [6.2], PVO = 21.1 [5.9]; t = 2.53, p < 0.05). Thus, despite being well matched on gender and ethnicity, the good outcome group had a later age at onset and more years of education, as expected on the basis of the prior literature. We then examined the neurocognitive archival data. We had degraded stimulus CPT data available on 25 GVO and 78 PVO; span of apprehension (SOA) data on 27 GVO and 94 PVO; WAIS-R subtest data on 27 GVO and 103 PVO; and neuropsychological test data on 22 GVO and 84 to 89 PVO (depending on the variable). It is important to note that these GVO–PVO proportions are not representative; these data were collected over several years and many PVO patients were never assessed. Specific descriptions of the CPT and SOA task parameters have previously been published (Strauss et al. 1993).

The WAIS-R and neuropsychological measures are shown in table 1, along with effect sizes (ES) for the
which presents the percentage of cases correctly classified in each group as well as the total correct classification results for each individual variable as seen in table 2, analyses (DFA) examining the correct classification beyond the influence of premorbid competence. Thus, there is evidence that neuropsychological performance is associated with vocational outcome, above and beyond the influence of premorbid competence, while deficits in others have important negative functional consequences. Four of the top five discriminators of GVO are measures involving processing speed, a construct rarely the focus of recent neuropsychological discussions of schizophrenia. The top four discriminators of PVO include measures of social problem solving and knowledge (PA, Comprehension), verbal ability (vocabulary), and response generation (verbal fluency); other than verbal fluency, few of these tests have been the focus of much discussion in the literature.

The GVO group clearly performed better than the PVO group on nearly every test, except for the degraded stimulus CPT and span of apprehension. The effect sizes differed from those that best classified PVO. For example, Trails B correctly classified 72.7 percent of GVO patients but only 42.4 percent of the PVO. Picture arrangement (PA) correctly classified 76.9 percent PVO, but only 42.4 percent of the PVO. Picture arrangement category; other than verbal fluency, few of these tests have been the focus of much discussion in the literature.

For example, Trails B correctly classified 72.7 percent of GVO patients but only 42.4 percent of the PVO. Picture arrangement category. Other than verbal fluency, few of these tests have been the focus of much discussion in the literature.

We next performed a series of discriminant function analyses (DFA) examining the correct classification results for each individual variable as seen in table 2, which presents the percentage of cases correctly classified in each group as well as the total correct classification rate. Variables are displayed in descending sensitivity to GVO.

Table 1. Differences in neuropsychological test performance between good vocational outcome (GVO) and poor vocational outcome (PVO) patients

<table>
<thead>
<tr>
<th>Test</th>
<th>GVO, mean (SD)</th>
<th>PVO, mean (SD)</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>V</td>
<td>9.5 (2.8)</td>
<td>7.8 (2.9)</td>
<td>0.57</td>
</tr>
<tr>
<td>C</td>
<td>8.6 (3.2)</td>
<td>6.7 (2.5)</td>
<td>0.74</td>
</tr>
<tr>
<td>PC</td>
<td>9.0 (2.6)</td>
<td>7.4 (2.8)</td>
<td>0.61</td>
</tr>
<tr>
<td>PA</td>
<td>9.4 (2.7)</td>
<td>7.2 (2.5)</td>
<td>0.87</td>
</tr>
<tr>
<td>VF</td>
<td>50.7 (14.0)</td>
<td>40.2 (13.1)</td>
<td>0.76</td>
</tr>
<tr>
<td>WC</td>
<td>4.3 (2.2)</td>
<td>2.9 (2.1)</td>
<td>0.68</td>
</tr>
<tr>
<td>WP</td>
<td>22.3 (14.9)</td>
<td>29.6 (20.1)</td>
<td>0.38</td>
</tr>
<tr>
<td>LM</td>
<td>21.0 (8.1)</td>
<td>16.2 (9.3)</td>
<td>0.53</td>
</tr>
<tr>
<td>VR</td>
<td>31.8 (6.7)</td>
<td>26.2 (8.1)</td>
<td>0.72</td>
</tr>
<tr>
<td>TA</td>
<td>38.9 (16.8)</td>
<td>45.8 (20.1)</td>
<td>0.35</td>
</tr>
<tr>
<td>TB</td>
<td>106.9 (54.6)</td>
<td>134.1 (83.7)</td>
<td>0.35</td>
</tr>
<tr>
<td>SW</td>
<td>90.6 (20.8)</td>
<td>76.5 (17.2)</td>
<td>0.79</td>
</tr>
<tr>
<td>SC</td>
<td>63.3 (15.7)</td>
<td>54.1 (13.0)</td>
<td>0.68</td>
</tr>
<tr>
<td>SCW</td>
<td>32.7 (9.2)</td>
<td>27.2 (9.4)</td>
<td>0.58</td>
</tr>
<tr>
<td>JL</td>
<td>23.6 (5.4)</td>
<td>20.9 (6.3)</td>
<td>0.44</td>
</tr>
<tr>
<td>CPT</td>
<td>2.23 (1.27)</td>
<td>2.38 (1.05)</td>
<td>0.14</td>
</tr>
<tr>
<td>SOA %</td>
<td>69.35 (10.29)</td>
<td>70.9 (10.3)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Note.—SD = standard deviation; V = vocabulary; C = comprehension; PC = picture completion; PA = picture arrangement; VF = verbal fluency; WC = Wisconsin Card Sorting Test (WCST) categories; WP = WCST percent perseverative error; LM = logical memory; VR = visual reproduction; TA = Trails A; TB = Trails B; SW = Stroop Word Reading; SC = color naming; SCW = interference condition; JL = judgment of line orientation; CPT = Continuous Performance Test; SOA = span of apprehension.

Table 2. Discriminant function analyses for classifying good vocational outcome (GVO) and poor vocational outcome (PVO) patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>GVO, % correctly classified</th>
<th>PVO, % correctly classified</th>
<th>Total, % correctly classified</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>59.3</td>
<td>66.1</td>
<td>64.7</td>
</tr>
<tr>
<td>VR</td>
<td>72.7</td>
<td>58.4</td>
<td>61.3</td>
</tr>
<tr>
<td>TA</td>
<td>72.7</td>
<td>51.2</td>
<td>55.6</td>
</tr>
<tr>
<td>TB</td>
<td>72.7</td>
<td>42.4</td>
<td>48.6</td>
</tr>
<tr>
<td>SW</td>
<td>71.4</td>
<td>62.0</td>
<td>62.4</td>
</tr>
<tr>
<td>SCW</td>
<td>71.4</td>
<td>62.5</td>
<td>64.2</td>
</tr>
<tr>
<td>WC</td>
<td>68.2</td>
<td>61.9</td>
<td>63.2</td>
</tr>
<tr>
<td>WP</td>
<td>68.2</td>
<td>46.4</td>
<td>50.9</td>
</tr>
<tr>
<td>V</td>
<td>66.7</td>
<td>67.0</td>
<td>66.9</td>
</tr>
<tr>
<td>LM</td>
<td>63.6</td>
<td>66.3</td>
<td>64.7</td>
</tr>
<tr>
<td>VF</td>
<td>59.1</td>
<td>63.9</td>
<td>67.3</td>
</tr>
<tr>
<td>CPT</td>
<td>56.0</td>
<td>52.6</td>
<td>54.3</td>
</tr>
<tr>
<td>JL</td>
<td>50.0</td>
<td>6.5</td>
<td>55.1</td>
</tr>
<tr>
<td>SOA</td>
<td>48.1</td>
<td>53.2</td>
<td>52.1</td>
</tr>
<tr>
<td>PC</td>
<td>44.4</td>
<td>66.1</td>
<td>61.8</td>
</tr>
<tr>
<td>SC</td>
<td>61.9</td>
<td>63.6</td>
<td>63.3</td>
</tr>
<tr>
<td>PA</td>
<td>59.3</td>
<td>76.9</td>
<td>73.3</td>
</tr>
</tbody>
</table>

Note.—C = comprehension; VR = visual reproduction; TA = Trails A; TB = Trails B; SCW = interference condition; SW = Stroop Word Reading; WC = Wisconsin Card Sorting Test (WCST) categories; WP = WCST percent perseverative error; V = vocabulary; LM = logical memory; VF = verbal fluency; CPT = Continuous Performance Test; JL = judgment of line orientation; SOA = span of apprehension; PA = picture arrangement.
classification rates were total, 70.8 percent, GVO, 81.0 percent, and PVO, 67.6 percent. This optimal solution contained picture arrangement, vocabulary, Stroop word reading, WCST categories and percent preservative error, and Trails B. Clearly, picture arrangement as a single variable is accounting for most of the classification success, given that it achieved a total correct classification rate of 73.3 percent by itself in the larger sample shown above, with the other variables mostly increasing sensitivity to GVO.

Two aspects of these results are particularly noteworthy. First, cognitive measures do appear to be robustly related to vocational outcome. Second, several of the variables most often studied in the schizophrenia literature, including the CPT and WCST, do not appear to have a unique relationship to functional outcome. Indeed, measures of processing speed and social judgment appear to be more discriminating. Of note, the two tests most often considered vulnerability markers (CPT and span of apprehension; Nuechterlein and Dawson 1984) did not appear to be related to outcome, consistent with the distinction between cognitive deficits related to risk and those related to illness presence (see below).

These data have a number of important limitations, expected of archival data that should temper our confidence in the results. Patient classification was done crudely and the cognitive data set has many missing values, limiting the sample size for some of the multivariate analyses. The results, however, demonstrate that it may be possible to correctly classify most GVO patients, a result of great clinical relevance. The delineation of a pattern of cognitive strengths associated with good outcome in schizophrenia could then be used to identify patients who are currently functioning poorly for more careful clinical evaluation. In essence, such patients appear to have "what it takes" but are not succeeding. In such cases, symptomatic features, which are not strongly related to vocational functioning in most studies, may be important and indicate a need for aggressive pharmacological treatment and enhanced psychosocial intervention. In addition, this type of data, if replicated, provides a rational and empirical framework for targeting cognitive functions for rehabilitative or pharmacological interventions with the hope of reducing the vocational disability common in the illness. An issue of interest here is whether it is more effective to build competencies related to success or to ameliorate deficits related to failure. This conceptual approach also suggests that patients lacking critical competencies may be in need of a different rehabilitation approach.

We next addressed the question of whether the robust neuropsychological differences between GVO and PVO patients might reflect differences in brain morphology. We identified a sample of GVO and PVO patients and normal controls from archival magnetic resonance imaging (MRI) data sets collected by Breier et al. (1992) and Buchanan et al. (1993). The MRI scans were obtained using a 1.5 T Siemens Magnetom scanner. The whole brain was evaluated in the coronal plane with 3-mm contiguous coronal sections, using the spin-echo technique with a TR of 600 milliseconds and TE of 17 milliseconds with two excitations and a 256 × 256 pixel matrix. Image analyses were performed using the Loats image analyses system. Details of measurement methods are described in the studies cited above. From the pool of available data, we individually matched right-handed GVO, PVO, and normal subjects for gender, race, and age (± 3 yrs). Each group comprised 10 males and 4 females. Mean ages (SDs) of the three groups were GVO, 34.54 (4.5); PVO, 33.58 (4.9); and normal controls, 36.04 (4.3). The results are presented in Table 3.

Although the groups had grossly similar total volumes for the temporal and frontal lobes, there appears to be a basic difference in the extent of cortical asymmetry. We contrasted the right and left temporal and frontal lobes of each group using matched-pair t tests. In normal controls, right frontal and right temporal lobes were larger than left ones (t = 3.39, p < 0.005 and t = 2.96, p < 0.011, respectively). The same asymmetry pattern was observed in the GVO group for the frontal and temporal lobes (t = 3.35 and t = 3.47, respectively; both p < 0.01). This asymmetry was absent in the PVO group (frontal lobe, t = 0.31; temporal lobe, t = -0.34). The PVO group apparently lacks normal cortical asymmetry patterns, a possible marker of neurodevelopmental compromise. Such findings of abnormalities of asymmetry have previously been reported in schizophrenia with a mixed history of replication (Luchins et al. 1982; Bilder et al. 1994; Flaum et al. 1995; Kulynych et al. 1995). Our data suggest that an abnormality of asymmetry is not necessarily characteristic of schizophrenia, but may be related to outcome.

We next examined amygdala-hippocampus (AHC) volumes and calculated effect sizes using the normal controls from archival magnetic resonance imaging (MRI) data sets collected by Breier et al. (1992) and Buchanan et al. (1993). The MRI scans were obtained using a 1.5 T Siemens Magnetom scanner. The whole brain was evaluated in the coronal plane with 3-mm contiguous coronal sections, using the spin-echo technique with a TR of 600 milliseconds and TE of 17 milliseconds with two excitations and a 256 × 256 pixel matrix. Image analyses were performed using the Loats image analyses system. Details of measurement methods are described in the studies cited above. From the pool of available data, we individually matched right-handed GVO, PVO, and normal subjects for gender, race, and age (± 3 yrs). Each group comprised 10 males and 4 females. Mean ages (SDs) of the three groups were GVO, 34.54 (4.5); PVO, 33.58 (4.9); and normal controls, 36.04 (4.3). The results are presented in Table 3.

Table 3. MRI comparisons of good vocational outcome (GVO) and poor vocational outcome (PVO) patients with normal controls (NC)

<table>
<thead>
<tr>
<th></th>
<th>PVO</th>
<th>GVO</th>
<th>NC</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFC-R</td>
<td>79.75 (17.25)</td>
<td>82.72 (16.61)</td>
<td>81.21 (10.91)</td>
</tr>
<tr>
<td>PFC-L</td>
<td>78.97 (15.35)</td>
<td>75.29 (13.87)</td>
<td>75.29 (10.26)</td>
</tr>
<tr>
<td>TL-R</td>
<td>56.66 (10.98)</td>
<td>56.46 (8.05)</td>
<td>58.98 (7.53)</td>
</tr>
<tr>
<td>TL-L</td>
<td>57.45 (9.16)</td>
<td>52.34 (7.63)</td>
<td>55.93 (7.99)</td>
</tr>
<tr>
<td>AHC-R</td>
<td>6.17 (0.61)</td>
<td>6.29 (0.99)</td>
<td>6.59 (0.60)</td>
</tr>
<tr>
<td>AHC-L</td>
<td>6.15 (0.59)</td>
<td>6.29 (0.88)</td>
<td>6.67 (0.60)</td>
</tr>
</tbody>
</table>

Note.—Group mean raw data (with standard deviation) are shown for total volume in cubic centimeters of the right (R) and left (L) hemisphere measurements of the prefrontal cortex (PFC), temporal lobe (TL), and amygdala-hippocampus (AHC).
trol standard deviation. Both patient groups demonstrated moderate to large effect sizes relative to controls, suggesting left AHC volume reduction (PVO ES = 0.86; GVO ES = 0.62), with somewhat less marked findings on the right (PVO ES = 0.70; GVO ES = 0.50; R+L GVO ES = 0.63; R-L PVO ES = 0.88). Thus, in contrast to cortical asymmetry, volume reduction of the amygdala-hippocampus does not appear to be related to outcome. Both groups demonstrate the finding, previously reported by multiple laboratories (Suddath et al. 1990; Falkai and Bogerts 1995; Pearlson et al. 1984). The fact that the GVO patients have smaller left temporal and frontal volumes than the PVO patients is incompatible with the view that the GVO group simply has a less severe form of the disease than the PVO group. Instead, these data suggest that subgrouping patients on vocational status reveals qualitative differences in brain morphology.

As with the cognitive data, we consider these MRI results to be preliminary but provocative. The results suggest that the large cognitive differences observed between outcome groups may reflect basic differences in brain morphology. The fact that the poor outcome patients appear to lack normal cortical asymmetries is not surprising when considered in the context of their poor neuropsychological performance.

These results have two implications to consider in schizophrenia rehabilitation. First, the fact that good outcome may be associated with particular patterns of brain morphology, as with the cognitive findings discussed above, is evidence that certain strengths and basic competencies may be critical for a good outcome in schizophrenia. It is important to be able to identify patients who appear to have these competencies, but are not currently functioning, for special clinical attention. Second, the fact that poor outcome is associated with greater abnormality of brain morphology is neither surprising—previous reports have documented relationships between poor outcome and ventricular size (Pearlson et al. 1984; Vita et al. 1991; van Os et al. 1995)—nor cause for nihilism. It appears likely that such patients may require very different services to achieve maximum independence than patients who have much more intact cognitive performance. However, such services cannot be developed effectively until we have achieved a clearer understanding of the determinants of disability in schizophrenia.

What Are the Upper Limits to Cognitive Enhancement?

While we are optimistic that our proposed research strategy will improve the prospects for effective rehabilitation, a number of findings reported in the literature since the 1992 *Schizophrenia Bulletin* At Issue series point to the challenges confronting interventions that are designed to enhance cognitive functioning. Further evidence has accumulated that many patients demonstrate subtle attentional, cognitive, and neuromotor abnormalities in early childhood, long before the onset of overt psychotic illness, in keeping with "neurodevelopmental" models of the illness (Cornblatt and Keilp 1994; Walker et al. 1994; Weinberger 1995).

Perhaps the most remarkable investigation demonstrating this trend was performed by Jones et al. (1994), who followed subjects originally studied as part of the Medical Research Council National Survey of Health and Development, a study of all births in England, Scotland, and Wales during the week of March 3–9, 1946. These children were assessed multiple times (beginning at 6 weeks) with measures of developmental milestones, educational achievement, and social-behavioral assessments. Of the 4,746 English subjects, 30 developed schizophrenia by the age of 43, with cases identified and diagnosed on the basis of multiple medical record sources, case registers, and direct interview data using an abbreviated Present State Examination when subjects were age 36. These subjects demonstrated delayed achievement of motor and speech milestones in infancy, lower estimated IQ scores by middle childhood, and increased social anxiety by early adolescence in comparison with the 4,716 controls. These data suggest that adult schizophrenia is preceded by multiple manifestations of subtle developmental compromise across neurological, intellectual, and social domains.

The intellectual and educational testing deficits observed in the Jones et al. (1994) study are statistically significant but small, in marked contrast to the *substantial* cognitive deficits found in samples of adult schizophrenia patients (Goldberg and Gold 1995). Thus, strong inferential evidence suggests that the extent of cognitive impairment (both breadth and severity) widens sharply with the onset of psychotic illness. Whether this change is a simple quantitative amplification of the early deficit pattern or involves a qualitative change suggesting the compromise of additional neural systems remains an unanswered but critical question for adequately conceptualizing the pathophysiology of cognitive impairment in schizophrenia. At this point it is reasonable to speculate that the impairments observed in adult patients are of at least two types: (1) those present from early in development, and (2) those related to clinical psychotic illness. The existence of such early, developmentally based impairments suggests that the concept of "premorbid" functioning in schizophrenia may no longer be tenable; rather, there is a preschizophrenic period characterized by subtle evidence of the "morbid" process. The challenge confronting attempts at cognitive
enhancement may not be "rehabilitation," which implies restoration of function, but instead the development of critical competencies and strategies for coping with deficits.

Consistent with the notion that cognitive impairment may be a risk marker for schizophrenia is the developing literature documenting subtle impairments in first-degree relatives of patients, suggesting that some types of cognitive impairment may mark the genetic phenotype (Cannon et al. 1994; Kremen et al. 1994; Faraone et al. 1995; Mirsky 1996). These data may also have important implications for rehabilitative approaches to schizophrenia, as some of the deficits observed in patients are the result of genetic factors, which are largely independent of clinical illness. Although patients may perform at lower levels than their relatives on some putative genetic risk markers, possibly as a consequence of the additional impairment that accrues with illness, such genetically mediated neurocognitive impairments may be fundamentally stable deficits. Following from this, it seems improbable (although not logically impossible) that any form of intervention is capable of enhancing the functioning of patients beyond the level of deficit seen in nonpsychotic relatives. There is likely a ceiling to how much improvement can be hoped for, a ceiling below the performance level of normal controls. Indeed, treatment-related enhancements that even approach this level would involve a remarkable degree of change in cognitive performance. Of course, this argument is conjectural and based on our short-term crystal ball. New medications or innovative rehabilitation techniques could, conceivably, produce greater remediation than currently seems possible.

The distinction between impairments linked to risk for illness and those related to presence of clinical illness has implications for the selection of treatment targets. The risk status of a patient cannot be changed: They were once at risk and now have developed the illness. Targeting the cognitive processes thought to reflect genetic risk would therefore be an unproductive strategy. For example, abnormalities of attention are clear in patients, and similar abnormalities (albeit perhaps of lesser severity) appear to be present in a large number of relatives who are not clinically ill and who manage to function in the social and vocational domains, as well as in prepsychotic children. It seems unlikely that attention training, such as that used in many settings with traumatic brain injury patients, would have great benefits for patients with schizophrenia. Instead, we propose that treatment targets be selected from among those impairments that are most evident in ill patients and where patients diverge most clearly from their nonpsychotic relatives.

A study consistent with this perspective was recently reported by Harris et al. (1996), who examined the neuropsychological performance of 14 patients with schizophrenia, their 28 parents, and a group of normal controls. Eight parents had a positive family history for schizophrenia but were married to a spouse with a negative family history. The attentional and learning/memory performance of the schizophrenia proband was compared with that of their parents using demographically corrected scores. The family history positive parents and their children demonstrated similar degrees of attention impairment relative to controls and to family history negative spouses. In contrast, the schizophrenia probands scored more poorly than either parent on learning/memory measures, suggesting a fundamental distinction between attention and memory impairments in terms of their relationship to genetic risk as opposed to clinical illness. Although this study is based on a very small sample, the results are provocative. If the goal is to enhance the cognitive function of patients with schizophrenia, it would seem logical to start with the deficits most clearly related to clinical illness, rather than those shared with nonpsychotic, functioning first-degree relatives.

Unfortunately, there is no shortage of potential rehabilitation targets. The literature since 1992 has clearly documented that "illness-related" impairments are quite broad on standard neuropsychological batteries. Thus, performance tends to be one or more standard deviations below normative levels across measures of attention, memory, problem solving, motor performance, language, and visual processing in many studies (Saykin et al. 1991, 1994; Braff et al. 1991). Although several demonstrations and discussions have centered on the possible differential impairment of memory, verbal memory particularly, memory impairment clearly occurs on the background of other deficits that may be only slightly less severe (Saykin et al. 1991; Gold et al. 1992; Tamlyn et al. 1992). Such results raise two possibilities: that (1) schizophrenia involves multiple discrete impairments, or (2) the general deficit pattern may be the result of a smaller number of specific impairments with broad consequences. These two perspectives have radically different implications for rehabilitation. The first possibility suggests that patients will require a very broad form of cognitive training, addressing most forms of complex cognition that are involved in everyday functioning. The second suggests that a more focused approach based on a conceptual model of the origins of general impairment could be more efficient and effective.

We (J.G.) have previously published data demonstrating that a measure of working memory (letter-number span) was highly correlated with Wisconsin Card Sorting Test performance in schizophrenia and that co-varying,
between-group working memory differences eliminated patient-normal control differences on the WCST (Gold et al. 1997). These results suggested that basic working memory deficits might account for the more complex problem-solving and "executive" function deficits in schizophrenia. Although that study focused on the WCST, the data also revealed substantial correlation between working memory and full scale IQ (FSIQ) ($r = 0.58$), Trails B ($r = -0.45$), and Wechsler Memory Scale—Revised General Memory Index ($r = 0.39$). Thus, working memory may in fact be a critical determinant of the general deficit in schizophrenia. Indeed this possibility is bolstered by the fact that working memory demonstrates a robust relationship to full scale IQ in the 2,450 normal subject standardization sample for the WAIS III; the letter-number sequencing correlation with FSIQ was 0.64 (Psychological Corporation 1997). Working memory appears to be a critical building block for many forms of cognition; an impairment in this function should have broad consequences. Although the available data mostly suggest that working memory has such a broad role, other variables may also be critical determinants of the general deficit in schizophrenia. For example, in the cognitive aging literature, Salthouse (1993) has demonstrated that perceptual processing speed may be the primary mediator of the broad age-related cognitive changes.

From a rehabilitation perspective, such findings may be cause for optimism: If it is possible to enhance (either pharmacologically or through a behavioral intervention) the cognitive processes that contribute to the generalized deficit, it may be possible to produce broad effects from a focused intervention. Clearly this remains an empirical question and challenge. However, we do think that expectations about the effects of cognitive rehabilitation and models of which cognitive functions may be critical in mediating impairment must be qualified by the substantial recent evidence that some impairment precedes psychosis, some impairments are found in good-functioning relatives, and illness-related neuropsychological deficits are superimposed on a background level of dysfunction.

**Conclusions**

The subject of cognitive impairment in schizophrenia, the role of such impairments in mediating disability, the impact of new pharmacological agents on cognition, and the possibility of psychosocial interventions to enhance cognitive performance have become central issues in the literature on schizophrenia, with interest growing rapidly since 1992. While much has been learned about these issues in the past 5 years, there has been modest progress, at best, in the development of rehabilitation strategies to improve in cognitive functioning. In our view, several important questions remain largely unanswered: (1) Which impairments are specifically related to different aspects of outcome? (2) Are there important individual differences in the type of rehabilitation strategy that may be effective? and (3) Does the enhancement of specific cognitive functions lead to larger clinical and functional benefits? We suggest that a new perspective on the selection of treatment targets, that is, the study of good outcome patients, may be more appropriate than current strategies for answering these questions.

The fact that schizophrenia is a heterogeneous disorder has had much more impact on discussions of diagnosis and etiology than on rehabilitation. Our data on work outcome suggest that important functional differences should be considered in planning treatment. This hypothesis is consistent with several recent studies on the WCST. As many as 20 percent of patients may perform within normal levels on the WCST, and poor-performing patients appear to have a broader pattern of neuropsychological deficits than those who can perform at normative levels (Braff et al. 1991; Goldstein et al. 1996). Stratta and colleagues (1997) suggest that there are important differences in how patients perform the task, as well as in how well they do. They subdivided patients into good and poor performing groups on the basis of categories correct at baseline, and then requested them to enumerate their selection strategy on readministration. The good baseline performers improved significantly with this technique, while the poor performers got worse. The additional task demand apparently further disrupted their already impaired ability to solve the task.

Until we can identify the most relevant targets for rehabilitation and determine which patients require which types of interventions, we propose that efforts at rehabilitation focus more on improving functional skills than on enhancing cognitive capacities. The extensive knowledge that has been accumulated about these underlying deficits should be used to guide the format and structure of functional skills training.

We have employed this strategy in a skills-based intervention for substance abuse by people with schizophrenia. Drug and alcohol abuse has become one of the most significant problems facing agencies and clinicians involved in treatment of people with schizophrenia. The lifetime prevalence rate of substance abuse in schizophrenia is close to 50 percent (Regier et al. 1990; Mueser et al. 1995b) and estimates of recent or current substance abuse range from 20 percent to 65 percent (Drake et al. 1989; Mueser et al. 1992). We have developed a treatment protocol containing four modules that are implemented sequentially: (1) social skills and problem-solving training
to enable patients to develop non–substance-using social contacts and to be able to refuse social pressure to use substances; (2) education about the reasons for substance use (e.g., habits, triggers, and craving) and the particular dangers of substance use for people with schizophrenia; (3) motivational interviewing and goal setting for decreased substance use; and (4) training in behavioral skills for coping with urges and high-risk situations. Several steps are taken in consideration of cognitive deficits. Sessions are highly structured and the predominant activity is behavioral rehearsal. The material is broken down into small units, and everything is supplemented by illustrative posters and handouts. Complex social repertoires required for making friends and refusing substances are divided into component elements such as maintaining eye contact and how to say “No.” Patients are first taught to perform the elements and then gradually learn to smoothly combine them. The intervention emphasizes overlearning of a few specific and relatively narrow skills that can be used automatically, thereby minimizing the cognitive load for decision making during stressful interactions. Extensive use is made of learning aids, including handouts and flip charts, to reduce memory and attention requirements. Patients are prompted as many times as necessary, and extensive repetition is used within and across sessions. Patients repeatedly rehearse both behavioral skills (e.g., refusing unreasonable requests) and didactic information (e.g., the role of dopamine in schizophrenia and substance use) and receive social reinforcement for effort. Training is done in a small group format (6–8) to ensure sufficient individual attention and opportunities to rehearse skills within the session.

Content on coping skills and relapse prevention is adapted from substance abuse programs based on social learning theory that have proven effective with less impaired patients (Marlatt and Gordon 1985; Annis and Davis 1995). However, rather than teaching generic problem-solving skills and coping strategies that can be adapted to a host of diverse situations, we focus on specific skills effective for handling a few key high-risk situations (e.g., what do you do when you are offered coke by your brother or by one specific friend, rather than what to do when anyone offers it to you). Similarly, goals and reasons for reduced use are very concrete and short term. “I want to stop using crack between today and the weekend” is more typical than “I need to use less crack.” Similarly, a modal reason for reduced use is avoiding arrest rather than “getting a good job and getting my life in order.”

Our subjects have been uniformly unable to generate abstract goals and reasons to reduce drug use. Consequently, we have recently added a urinalysis contingency in which patients receive money if they have clean urine samples. This reward serves to increase the salience of the weekly goal. Anecdotal reports from patients and their primary clinicians suggest that they retain and employ the information and skills we teach between sessions. Nevertheless, they continue to exhibit deficits in abstraction and in the ability to apply newly learned skills to novel situations, even in simulated interactions during sessions. It remains to be determined whether these compartmentalized skills will be effective in reducing substance use or if a more generalizable set of coping abilities is required.

In conclusion, we remain optimistic that effective rehabilitation techniques can be developed and that the most efficacious strategy for enhancing community functioning involves complementary psychopharmacological and psychosocial approaches. We also believe that cognitive impairments are central to the illness and must be taken into account in planning treatment and evaluating treatment outcome. However, we believe that (a) the neurodevelopmental nature of the impairments defies simple solutions and (b) cognitive rehabilitation strategies that depend primarily on repeated practice of neuropsychological tasks are unlikely to yield much improvement in the underlying cognitive operations (e.g., working memory) or have much benefit for community functioning.

References


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Acknowledgment

Preparation of this manuscript was supported by U.S. Public Health Service grants DA09406 from the National Institute of Drug Abuse (A.S.B.); MH-40279 (J.M.G. and R.W.B.) and MH-48225 (R.W.B.) from the National Institute of Mental Health; and grants from the National Alliance for Research on Schizophrenia and Depression, the Stanley Foundation, and MH-57749 (J.M.G.).

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