Cognitive Functioning in Schizophrenia: Implications for Psychiatric Rehabilitation

by William D. Spaulding, Shelley K. Fleming, Dorie Reed, Mary Sullivan, Daniel Storzbach, and Mona Lam

Abstract

Research in psychopathology and the cognitive neurosciences suggests new applications in psychiatric rehabilitation. Analysis of performance deficits on laboratory tasks can contribute to treatment planning, individual and family counseling, and staff consultation, much like it does in cases of brain injury and other types of central nervous system neuropathology. Recognition of the nature of cognitive impairments in schizophrenia can inform design of psychosocial techniques such as social and living skills training. Cognitive impairments are increasingly seen as potential targets for pharmacological and psychosocial treatment and rehabilitation. In this article, three key issues for application of cognitive technology in psychiatric rehabilitation of schizophrenia and related disorders are formulated as straightforward, clinically relevant questions: (1) What is the prognostic significance of cognitive impairment in acute psychosis? (2) Can cognitive functioning improve in the chronic, residual course? (3) How does cognitive improvement benefit other aspects of recovery and rehabilitation? These questions are addressed through review of previous findings and new multivariate analyses of cognitive functioning in the acute, post-acute, and chronic residual phases of schizophrenia.

Key words: Cognitive rehabilitation.


Historically, the preponderance of scientific interest in the cognitive aspects of schizophrenia has been directed toward illuminating the disorder's etiology, with only indirect consideration of clinical applications. Nonetheless, cognitive measures and models are increasingly proposed as potentially useful prognostic indicators (Wykes et al. 1990; Wykes and Dunn 1992; Bowen et al. 1994), as limiting factors in social functioning (Penn 1991; Kern and Green 1994; Penn et al. 1995, 1996; Green 1996; Meltzer et al. 1996), and as targets for direct treatment (Brenner et al. 1983, 1992; Spaulding et al. 1986, 1998; Corrigan and Storzbach 1993; Lee et al. 1994). These proposals reflect a convergence, on the one hand, of research in the neurosciences, experimental psychopathology, neuropsychology, and cognitive-behavioral psychotherapy and, on the other hand, a perceived need to translate the methods, principles, and insights of cognitive psychopathology into practice.

New roles for cognitive psychopathology suggest new applications for a number of familiar clinical technologies in the domain of psychological and neuropsychological assessment. For example, analysis of performance deficits on laboratory tasks can contribute to treatment planning, individual and family counseling, and staff consultation, much like it does in cases of brain injury and other types of central nervous system neuropathology (Erickson and Binder 1986; Erickson 1988, 1994). Similarly, recognition of the nature of schizophrenic cognitive impairments can inform design of psychosocial techniques such as social and living skills training (Liberman et al. 1982; Kern and Green 1994).

The issues for application of cognitive technology are not necessarily the same as those that drive development of etiological models. Also, the issues raised by cognitive applications in classical neuropsychology do not overlap completely with issues raised in assessment and treatment of schizophrenic impairments. For example, some parameters that give necessary context to traditional neuropsychological assessment, such as time since injury, are poorly understood and possibly irrelevant in schizophrenia.

In the following sections, three key issues applicable to psychiatric rehabilitation of schizophrenia and related disorders are formulated as straightforward, clinically relevant questions:

Reprint requests should be sent to Dr. W.D. Spaulding, Dept. of Psychology, University of Nebraska–Lincoln, Lincoln, NE 68588-0308.
1. What is the prognostic significance of cognitive impairment in acute psychosis?
2. Can cognitive functioning improve in the chronic, residual course?
3. How does cognitive improvement benefit other aspects of recovery and rehabilitation?

Recent research findings from our laboratory and others are marshaled to help clarify the nature of the questions and in some cases provide preliminary answers. In some instances, contemporary theoretical frameworks are helpful or even essential for informing application strategies. Neurodevelopmental models of schizophrenia (e.g., Walker 1994; Weinberger and Lipska 1995; Weinberger 1996) are especially important in this regard. In other instances, clinical considerations, observations, or imperatives suggest a need for further development of theoretical models. In the final section we propose theoretical models to account for the important new finding that cognitive impairments respond to psychosocial interventions in the chronic course of schizophrenia.

What Is the Prognostic Significance of Cognitive Impairment in Acute Psychosis?

Gross disruption of cognitive functioning is usually part of the clinical picture of acute psychosis, and reduction of cognitive impairment usually accompanies resolution of the acute episode. Experimental studies of the relationship between symptomatology and cognitive functioning in acute psychosis may provide clues about the neurophysiological and neuropsychological mechanisms that produce them (e.g., Gilbertson et al. 1994). However, what is known about the long-term prognostic significance of cognitive impairment is generally limited to the severity of residual impairment after resolution of acute psychosis (for a review, see Meltzer et al. 1996). Cognitive functioning at the point of hospitalization has been found to predict some important consequences, for example, emotional blunting after remission of the acute psychosis (Silverstein et al. 1994), but little more is known about the portent of cognitive functioning during exacerbations. Hospitalization during acute psychosis is often the starting point for long-term treatment and rehabilitation. A better understanding of the prognostic implications of cognitive functioning at this point could enhance the planning process.

To determine whether cognitive measures during an acute episode have prognostic value over and above diagnostic, symptomatic, and behavioral indicators, we reanalyzed data collected in a recent study of patients admitted to an acute short-term unit in a State hospital (Lam 1997).

During the study, 31 patients were admitted, and subsequently discharged or transferred to a long-term inpatient unit; 19 (61%) had a diagnosis of schizophrenia, 10 (32%) had a diagnosis of major depression or bipolar disorder, 1 had an eating disorder, and 1 had substance abuse-related psychosis. Each was assessed with a structured interview, the Brief Psychiatric Rating Scale (BPRS; Ventura et al. 1993); a self-report symptom and problem inventory, Symptom Checklist-90R (SCL-90R; Peveler and Fairburn 1990); and a neurocognitive test battery (COGLAB; Spaulding et al. 1989). Assessment was performed twice: within 14 days of hospitalization and 4 weeks later. Two assessments were included to determine whether cognitive functioning at the start of treatment has different prognostic significance than later. Two indices of short-term outcome were analyzed: length of stay in the acute unit and discharge destination. The latter is the setting to which the patient went upon discharge, coded as a scale reflecting graduated levels of restrictiveness from independent living to locked, long-term inpatient care.

With data available at the first assessment, including demographic characteristics, it was possible to construct a multiple regression equation that predicted about 65 percent of the variance in length of stay (adjusted $R^2 = 0.647$, $F = 11.28, p < 0.00005$). The regression statistics for this formula are shown in table 1. Interestingly, diagnosis is not significantly associated with outcome in this context. The patient's age, age at onset, and marital status are powerful predictors of length of stay; a BPRS and an SCL-90R subscale also contribute to a statistically significant degree. Even after those factors are taken into account, the perseverative error score on the COGLAB card sorting task contributes uniquely to the prediction. That is the only score of the 11 derived from the COGLAB battery that was associated with outcome, but the size of its beta weight is sufficient to allow confidence that it is not an artifact of multiple correlational tests.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta</th>
<th>Significance $^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.34</td>
<td>0.0248</td>
</tr>
<tr>
<td>Age at onset</td>
<td>0.39</td>
<td>0.0057</td>
</tr>
<tr>
<td>Marital status</td>
<td>0.56</td>
<td>0.0002</td>
</tr>
<tr>
<td>BPRS paranoia factor</td>
<td>0.31</td>
<td>0.0126</td>
</tr>
<tr>
<td>COGLAB Card Sort perseverative errors</td>
<td>0.52</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

$^1$Significance of $T$, reflecting the probability that the variable's unique contribution to the overall prediction of the dependent variable is zero.

Table 1. Multiple regression statistics for predicting length of stay from demographic, clinical, and cognitive characteristics at admission.

Note.—BPRS = Brief Psychiatric Rating Scale.
The demographic variables were not so effective for predicting discharge destination, but card sorting performance was (see table 2). The equation still accounted for 37 percent of the variance in discharge destination (adjusted $R^2 = 0.365, F = 4.34, p < 0.006$). These analyses indicate that patients with more impaired card sorting performance shortly after acute hospitalization stayed in the acute ward longer and were more likely to be discharged to a residential or long-term hospital unit than to supported or independent community living.

Data from the second assessment were then analyzed for additional predictive value. The contribution of age was eclipsed by other predictors at the second assessment, so it was excluded from the prediction equation. Card sorting performance at the second assessment no longer contributed either, but another COGLAB measure—performance on a backward visual masking task—did contribute. The best equation including these variables, and the remaining variables from the first assessment, accounted for almost 75 percent of the variance in length of stay (adjusted $R^2 = 0.744, F = 17.28, p < 0.00005$). As table 3 shows, card sorting performance at the first assessment and masking performance at the second assessment contributed uniquely to this prediction.

It is interesting that both paranoid behavior and card sorting perseverative errors contributed to outcome in this situation. Perseverative errors have long been associated with paranoia (Spaulding 1978), presumably because the rigidity of thinking that produces this type of error also produces the inflexible beliefs and attributions of paranoia. (The perseverative error score here uses the original criteria of the Wisconsin Card Sorting Task (WCST), which are different from the criteria used by WCST versions in most common use today; see Wagman and Wagman 1992). Perseverative errors as scored by the current criteria may be differentially associated with schizophrenia, but they are not necessarily associated with paranoia.) It would make sense that a syndrome of rigid thinking and hostile, suspicious, and uncooperative social behavior would inhibit efficacious treatment and disposition in a psychiatric treatment setting, but the current analyses indicate that the behavioral and the cognitive aspects of this syndrome contribute independently to outcome. The role of the masking measure at the second assessment is also interesting. Masking measures an early stage of visual information processing, but it is known to be responsive to antipsychotic drug interventions (Braff and Sacuzzo 1982). In this analysis, the masking measure may be detecting a subgroup of patients who respond less well to antipsychotic medication, who remain more actively psychotic after several weeks of treatment, and who therefore require a longer hospitalization.

These analyses provide some encouragement that cognitive assessment in the acute and early post-acute phase can be made useful for predicting post-acute and chronic baseline functioning, at least to the degree that length of hospital stay and discharge destination reflect baseline functioning. This prediction is likely to be easier in a mixed sample that includes patients with both high and low levels of baseline functioning. Within a group of patients with more impaired baseline functioning, higher levels of symptoms between episodes, and suboptimal medication response, it may be extremely difficult to predict baseline and residual levels of cognitive impairment. It may be difficult even to determine when the patient has reached stabilization of the acute state. In such cases, systematic longitudinal assessment may be necessary to determine the significance of cognitive impairments for longer-term treatment planning.

Table 2. Multiple regression statistics for predicting discharge destination from demographic, clinical, and cognitive characteristics at admission

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.11</td>
<td>0.5434</td>
</tr>
<tr>
<td>Age at onset</td>
<td>0.03</td>
<td>0.8519</td>
</tr>
<tr>
<td>Marital status</td>
<td>0.03</td>
<td>0.8687</td>
</tr>
<tr>
<td>BPRS paranoia factor at admission</td>
<td>0.51</td>
<td>0.0025</td>
</tr>
<tr>
<td>COGLAB Card Sort perseverative errors</td>
<td>0.43</td>
<td>0.0100</td>
</tr>
</tbody>
</table>

Note.—BPRS = Brief Psychiatric Rating Scale.

1Significance of $T$, reflecting the probability that the variable's unique contribution to the overall prediction of the dependent variable is zero.

Table 3. Multiple regression statistics for predicting length of stay from demographic, clinical, and cognitive data available after 6 weeks of hospitalization

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset</td>
<td>0.24</td>
<td>0.0234</td>
</tr>
<tr>
<td>Marital status</td>
<td>0.45</td>
<td>0.0001</td>
</tr>
<tr>
<td>BPRS paranoia factor at admission</td>
<td>0.28</td>
<td>0.0104</td>
</tr>
<tr>
<td>COGLAB Card Sort perseverative errors at admission</td>
<td>0.49</td>
<td>0.0001</td>
</tr>
<tr>
<td>COGLAB Backward Masking task at second assessment</td>
<td>0.41</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

Note.—BPRS = Brief Psychiatric Rating Scale.

1Significance of $T$, reflecting the probability that the variable's unique contribution to the overall prediction of the dependent variable is zero.
Can Cognitive Functioning Improve in the Chronic, Residual Course?

Apart from those examining treatment of residual depression or negative symptoms (e.g., Plasky 1991; Silver and Nassar 1992; Siris 1994), there are relatively few systematic studies showing cognitive recovery independent of resolution of acute psychosis ("recovery" in this context means regaining some degree of premorbid functioning, not necessarily full return to premorbid levels). Studies of long-term outcome of schizophrenia and related disorders (Harding et al. 1992) have found surprisingly high levels of recovery of personal and social functioning, indirectly suggesting that some degree of cognitive recovery underlies this. On the other hand, long-term behavioral recovery could also reflect the cumulative effects of socialization uninterrupted by acute episodes, without any changes in cognition per se. The atypical antipsychotics, especially risperidone, may produce somewhat better cognitive functioning than typicals in stabilized patients (Green 1998). This finding suggests the possibility of some remediation independent of episode resolution, and the search is on for pharmacotherapeutic strategies that minimize residual impairment while maximizing stabilization and symptom control. Meanwhile, the search also continues for psychosocial strategies to counteract residual cognitive impairment.

A previous analysis in our laboratory (Spaulding 1993) of 110 severely disabled but stabilized patients in a State hospital long-term unit showed that cognitive functioning undergoes little or no change over a 6-month period. A more recent longitudinal study, also completed in our lab (Spaulding et al. 1998), assesses cognitive changes in equally disabled and stabilized chronic patients over the same time period but in an enriched psychosocial treatment environment. The second study showed improvements in 9 of 12 measures of cognitive functioning in chronic schizophrenia patients with especially severe residual impairments. Measures of memory and executive functioning showed improvement, while measures of reaction time and continuous attention did not. One measure of preattentual visual processing—backward masking—changed, while another measure of preattentual processing—a span of apprehension task—did not. Thus, there is evidence that at least under certain conditions, some aspects of impaired schizophrenic cognition are subject to improvement in the chronic course.

What is the qualitative nature of the observed cognitive change? Are some aspects of cognitive functioning more amenable to recovery than others? Does the improvement simply reflect a general, overall improvement in neurophysiological, cognitive, and behavioral functioning? Do patients use less impaired abilities to help recover more impaired ones? The answers to these questions would provide important clues about how cognitive recovery can come about.

For the present article, in order to further articulate the nature of the cognitive changes observed in the Spaulding et al. (1998) study, we performed a principal components analysis of the data from that study. The analysis included change scores for the nine measures that showed a change over the 6-month study period. The change scores are simply the arithmetic difference between pre and posttreatment scores adjusted for initial values effects by residualization in linear regression (a statistical procedure to control for the problem that change scores may have different meanings at different levels of a measure). The results are summarized in table 4.

Using conventional extraction and rotation parameters, the analysis identifies three separate sources of variance that collectively account for about half of the total variance in cognitive change. Although there is some overlap, the three factors clearly differentiate changes in different domains of functioning. The first factor is predominantly a verbal processing factor that spans elemental and complex levels of cognition. (The backward masking task requires subjects to identify alphanumeric characters presented in a preattentional time frame, while verbal memory tasks require integrated storage and

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**Table 4. Structure matrix of neurocognitive change scores, oblique rotation of principal component extraction**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Factor 1</th>
<th>Factor 2</th>
<th>Factor 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rey Verbal Learning Test -Visual</td>
<td>0.76</td>
<td>0.12</td>
<td>0.01</td>
</tr>
<tr>
<td>COGLAB Backward Masking</td>
<td>0.75</td>
<td>0.00</td>
<td>0.09</td>
</tr>
<tr>
<td>Denman Verbal Memory Quotient</td>
<td>0.55</td>
<td>0.41</td>
<td>0.25</td>
</tr>
<tr>
<td>Rey Verbal Learning Test -Auditory</td>
<td>0.46</td>
<td>0.42</td>
<td>0.07</td>
</tr>
<tr>
<td>Halstead Reitan Trailmaking B</td>
<td>0.09</td>
<td>0.79</td>
<td>0.25</td>
</tr>
<tr>
<td>Halstead Reitan Tactile</td>
<td>0.07</td>
<td>0.71</td>
<td>0.17</td>
</tr>
<tr>
<td>Denman Nonverbal Memory Quotient</td>
<td>0.49</td>
<td>0.60</td>
<td>-0.33</td>
</tr>
<tr>
<td>COGLAB Card Sorting Task</td>
<td>0.00</td>
<td>0.27</td>
<td>0.77</td>
</tr>
<tr>
<td>Halstead Categories</td>
<td>0.37</td>
<td>0.15</td>
<td>0.76</td>
</tr>
</tbody>
</table>

1The Rey Verbal Learning Test in its standard form uses auditory presentation of the stimulus words. The nonstandard visual form uses presentation of printed words. Change scores are residualized for initial values (i.e., the effect of the initial overall severity of the impairment has been statistically removed).
retrieval of verbal information in a much longer time frame, in both visual and auditory modalities.) The second factor is a spatial information processing factor (all the tasks require processing of spatial relations, whether or not memory is also involved), and the third is a concept formation and manipulation factor. These results indicate that, in addition to the predominance of more global changes, cognitive change in the chronic residual phase is somewhat segregated into verbal, spatial, and conceptual domains.

Segregation of verbal and spatial functions suggests lateralized hemispheric differences. The findings on lateralized neuropsychological deficits in schizophrenia (Gruzelier 1979, 1991; see also Gold et al. 1994) suggest that both right and left lateralization can occur in a heterogeneous schizophrenia population. The segregation of verbal and nonverbal performance into separate factors, as in the table 1 factor structure, would be consistent with a mixed population of individuals with varying degrees of impairment lateralized to one or another cerebral hemisphere. However, the segregation of cognitive processes into factors could also reflect purely functional relationships between various aspects of behavioral performance, independent of hemispheric or any other kind of anatomical localization. They could also reflect relationships between specific cognitive abilities and anatomically dispersed neurophysiological mechanisms (e.g., neurotransmitter or neuroendocrine systems). Changes in these cognitive abilities could reflect slowly occurring changes in lateralized neurophysiological processes, or functional organization of cognitive processes, or combinations of the two.

Interestingly, Factors 1 and 2 are inversely correlated ($r = -0.23$), meaning improvement on one is associated with a lack of improvement, or deterioration, on the other. This correlation could occur because in patients with lateralized impairments, recovery from episode-linked deficits in the more impaired hemisphere is quantitatively greater, and therefore more apparent on neuropsychological tasks, or because vulnerability-linked deficits prevent recovery in the more impaired hemisphere. Also, there may be "trade-offs" involved in recovery processes. In Factor 3, there appears to be such a trade-off between nonverbal memory and concept manipulation performance, evidenced by the negative factor loading of the nonverbal memory measure. Such a trade-off could be the result of reallocating limited processing capacity from one functional domain to another (Knight and Russell 1978; Gjerde 1983). In that sense, cognitive recovery may in part represent more efficient allocation of cognitive capacity in response to environmental demands. In cases where there are significant enduring deficits, reallocation of capacity would be further improved by taking one's own strengths and weaknesses into account. If enduring deficits were lateralized, better executive reallocation would produce inverse relationships, as with Factors 1 and 2.

To further explore the implications of lateralization, we identified left- and right-lateralized deficits in this sample with a crude but clinically useful convention, a difference between Wechsler Adult Intelligence Scale 1981 (WAIS) Vocabulary and Picture Arrangement of three standardized subscale points in either direction. With this criterion, 34 percent of the sample showed lateralization to the right hemisphere, and 12 percent showed lateralization to the left. The patients with left lateralization had a strikingly poor outcome. Whereas the entire sample showed significant gains in social competence as measured by the Assessment of Interpersonal Problem Solving Skills (AIPSS; Donohoe et al. 1990) over the course of the study (discussed further below), the subgroup of left-lateralized patients showed no change.

Explicit targeting of cognitive impairment in psychosocial rehabilitation enhances cognitive improvement. The Spaulding et al. (1998) outcome study included a randomized controlled comparison of comprehensive biopsychosocial rehabilitation with and without a group treatment modality designed to exercise cognitive abilities believed to be prerequisite to sociobehavioral functioning. The modality was constructed from the cognitive subprograms of Integrated Psychological Therapy (IPT; Brenner et al. 1994), which combine social skills training with other psychosocial techniques. Control subjects received supportive group therapy in identical doses, and all subjects received a standard regimen of intensive pharmacotherapy, social and living skills training, contingency management, and other rehabilitation modalities. Over the course of 6 months of rehabilitation, patients who received the cognitive treatment showed improvement in some domains of cognition, but the subjects receiving intensive rehabilitation without the cognitive component did not. There was strong evidence for differential improvement in span of apprehension, a preattenttional level of cognitive processing. (The overall change on this measure was not significant because of the complete lack of improvement in the control subjects, and so this measure was not included in the factor analysis of changes described above.) This particular domain of cognition is known to be sensitive to "top-down" information processing factors (Silverstein et al. 1996), so it is possible that the differential improvement reflects better executive-level modulation of preattenttional processing routines, as opposed to improvement in the rate or efficiency of the routines themselves. There was weaker evidence of differential change in more global cognitive functions, as measured by the COGLAB card sorting task. In the con-
text of the large improvements in global functions in both
groups, further enhancement by cognitive treatment in
this domain may be less significant, or simply more diffi-
cult to detect. Taken together, these findings suggest that
part of the effect of the cognitive treatment was to con-
tribute a unique effect on the ability of higher-level func-
tions to optimally activate specialized elemental processes
in response to particular environmental demands.

In summary, cognitive recovery can occur in stabi-
lized patients, and it appears to involve a spectrum of spe-
cific processes. Generally, the changes appear more
robustly in higher levels of cognition. For both post-acute
and chronic course recovery, the predominance of
changes in measures of more complex cognition in the
available research data is consistent with the hypothesis
that recovery primarily involves improvements in execu-
tive-level organization, modulation, and integration of
 elemental cognitive processes, as opposed to better oper-
tion of the elemental processes themselves. (Medication-
related improvement in backward masking may be a sig-
nificant exception to this rule.) Differential recovery of
different brain functions, related to each other through
anatomical, neurophysiological, or functional organiza-
tion, may produce individual differences in the recovery
process as well. Lateralization of impairments may be
especially significant in this regard. Recovery is subject
to enhancement by environmental and psychosocial fac-
tors, which may range from “therapeutic milieu” condi-
tions to therapeutic procedures that explicitly target cog-
nitive functioning.

How Does Cognitive Improvement
Benefit Other Aspects of Recovery and
Rehabilitation?

Whether or not cognitive change can be enhanced by
treatment and rehabilitation, it is important to know
whether recovery of specific functions has meaningful
benefits for the patient. Such benefits could logically lie
in either objective or subjective domains. Subjectively, it
would be logical to expect that better cognitive function-
ing would be associated with reductions in distress or
greater self-efficacy. However, it would be difficult to
demonstrate this empirically because subjective expres-
sions could be influenced by many factors, including
symptom reduction and improvement in behavioral func-
tioning unrelated to cognitive changes. The systematic
studies needed to determine the true subjective value of
cognitive recovery in schizophrenia have not been per-
formed.

Many experimental and case studies show perfor-
ance improvements in cognitive domains in response to
practice, special training, or other treatment-like proce-
dures (reviewed by Reed et al. 1992; Corrigan and
Storzbach 1993). There can be little doubt that people
with stabilized chronic schizophrenia can achieve perform-
ance improvements on a variety of cognitively challeng-
ing tasks. However, the improvements observed in previ-
ous 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 eco-
logically significant benefits in personal or social func-
tioning. The Spaulding et al. (1998) study is the first
large-scale controlled treatment trial to show that treat-
ment-induced cognitive changes in the chronic phase have
important objective benefits.

The primary outcome measure in that study, the
AIPSS, is an elaborate assessment of social competence.
In the AIPSS, the subject is shown a series of videotaped
vignettes of people engaged in some interpersonal prob-
lem or conflict. After each vignette the subjects are inter-
viewed to ascertain their understanding of the portrayed
problem and their ability to resolve it. Finally, they are
asked to role-play a solution. The entire assessment is
itself videotaped and later scored by trained observers
using a structured protocol. Assessments like the AIPSS
detect improvements in social competence that are known
to have implications for long-term outcome, including
relapse and hospital recidivism (Wallace and Liberman
1985; Hogarty et al. 1987). The size of the treatment
effect of the cognitive intervention, as measured by the
AIPSS, is comparable to the effect size of atypical
antipsychotics over typicals in suppressing symptoms and
enhancing behavioral functioning. Longer-term appraisal
of overall rehabilitation outcome (Weilage 1997) confirms
that the Spaulding et al. (1998) cognitive treatment group
showed higher levels of rehabilitation success, as mea-
sured by judgment of staff who were blind to treatment
group assignment.

There are a number of possible causal relationships
between the domains of functioning measured in the
Spaulding et al. (1998) study. Cognitive changes may be
links in a cascade of changes, from stabilization of the
neurophysiological level of acute psychosis to social
behavior, or they may be incidental “markers” of neuro-
physiological changes, unrelated to behavioral conse-
quences. In addition to having different roles in the
causal sequence of recovery, beneficial effects of cogni-
tive recovery may logically be expected to be direct or
indirect. The latter would require interaction with some
other condition. For example, improvement in specific
attentional or memory capabilities may have no direct
effects on behavioral functioning, but may nevertheless
enhance a patient’s response to social skills training or
related rehabilitation interventions. This could be because
the cognitive abilities in question have limited importance to ongoing performance of social skills but are critical to acquisition or reacquisition of those skills.

For the purposes of this article, we conducted a series of analyses to explore in greater detail the mechanisms of the cognitive treatment effect reported by Spaulding et al. (1998). The first step in these analyses was to identify all statistically significant bivariate correlations between the degree of improvement in social competence and measures of cognition, behavioral functioning, and symptoms. The measure of social competence change is the change score on the AIPSS overall performance scale, residualized by linear regression to remove variance attributable to the initial value of the score. Five measures of clinical status (the five factors of the BPRS) and 13 neurocognitive measures were analyzed as predictor variables. The initial value and the residualized change score for each brought the total in the predictor pool to 36. Five of the pretreatment measures and two residualized change scores showed significant correlations with the AIPSS change score \( p < 0.05, \) uncorrected for multiple correlations. In addition, as expected from the significant cognitive treatment effect, the amount of cognitive treatment provided (expressed as a dose unit of 0 or 1, reflecting whether or not the patient received 6 months of cognitive treatment) was correlated with AIPSS change. Together, these eight measures account for about 21 percent of the total change in AIPSS performance (adjusted \( R^2 = 0.206, p < 0.0036 \).

The measures fall in four separate domains: four measures of cognitive functioning at the start of treatment, one measure of behavioral functioning before and during treatment (the Nurses Observation Scale for Inpatient Evaluation (NOSIE-30) Total Assets Scale; Honigfeld et al. 1966), two measures of change in cognitive functioning, and the "dose" of cognitive treatment.

The sequence and direction of possible causal relationships among measures in the different domains can be logically assumed; for example, the sequence of pretreatment functioning, administration of treatment, and changes during treatment is known. This allows construction of the path model shown in figure 1. A path model is a sequentially ordered set of multiple regression formulae constructed to represent causal, as opposed to merely correlational, relationships among variables. The strengths of such relationships are expressed as beta weights, as in conventional multiple regression, and they represent the unique contribution of each independent variable to the dependent variables. When causal sequences are unknown, alternative path models can be constructed and evaluated to determine which model best fits the available correlational data. When the possible causal pathways are constrained by a known sequence of events in real time, as in the present case, the path model that best fits the available data can provide information about how specific sets of variables influence an outcome.

The path model in figure 1 shows that the amount of cognitive treatment (i.e., the "dose" of cognitive therapy, expressed as a dosage unit of 1 or 0) directly influences AIPSS performance, without mediation by any of the cognitive measures in the protocol. This means that whatever the cognitive mechanism of the treatment effect may be, it is not identified in this model. Changes in COGLAB card sorting random errors and performance on the Halstead Reitan Trailmaking-Test B (Trails B) (Goldstein 1991) performance are also associated with AIPSS change, but this happens independently of the cognitive treatment. Trails B change is associated in turn with pretreatment levels of the visual form of the Rey Verbal Learning Test (VLT; Kern and Green 1994) and the false alarm rate on the COGLAB continuous performance test/Span of Apprehension Test. The sizes of the correlations do not permit much confidence in the relative contributions of the pretreatment variables or the Trails B change. The contributions of the card sorting change score and treatment type, however, do permit a confident conclusion that these two variables are independently associated with change in AIPSS performance. This would be consistent with (but does not prove) the hypothesis that improvements in the cognitive functions measured by the card sorting task enhance acquisition of social competence in the course of rehabilitation. However, what is most significant about this analysis is what it does not show: The cognitive treatment effect does not operate through any of the measured cognitive functions, and so its cognitive mechanisms remain unknown.

The final step in these analyses was to employ interaction terms (Downs and Robertson 1991; Cortina 1993) as independent (predictor) variables. An interaction term in this context is the arithmetic product of a quantitative expression of the treatment condition (the quantitative "dose" of treatment) and any organismic variable (e.g., a measure of cognitive functioning). The organismic variable can be analyzed as it existed at the outset of treatment, or it can be converted to a change score, that is, the difference between pre and posttreatment scores. When included as an independent (or "predictor") variable in a multiple regression equation whose dependent (or "target") variable is also a change score, the interaction term shows how the two different factors (the treatment and the organismic variable) work together to produce change. Interaction terms allow the possibility that a variable may behave differently in the presence of another variable. For example, cognitive functioning may affect acquisition of social competence only in the presence of cognitive treatment. This contrasts with conventional multiple regression, which can show only the unique contributions of the
individual variables. Interactions are assumed to operate over the course of the treatment period, so regression values cannot be ordered or sequenced, as in a path model. However, a single regression formula can be constructed that includes change scores, interaction terms, and treatment dose, and indicates how those factors work together over time.

In the Spaulding et al. (1998) data, 36 residualized change scores can be computed including interactions between treatment and pretreatment measures, and inter-
actions between treatment and residualized change scores. Five of these were found to have significant bivariate correlations with the AIPSS change score, and four are interactions between pretreatment cognitive functioning and treatment. The fifth is an interaction between changing cognitive functioning and treatment. A multiple regression equation including these, the card sorting and Trails B change scores, and treatment dose accounts for about 28 percent of the change in the AIPSS (adjusted $R^2 = 0.275$, $p < 0.0003$). The regression statistics are summarized in table 5.

Table 5. Multiple regression statistics for prediction of AIPSS change (residualized to remove initial value effects) by interaction terms, cognitive change, and treatment dose

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose of cognitive treatment</td>
<td>0.25</td>
<td>0.018</td>
</tr>
<tr>
<td>Change on COG LAB Card</td>
<td>0.18</td>
<td>0.090</td>
</tr>
<tr>
<td>Sort task</td>
<td>0.13</td>
<td>0.214</td>
</tr>
<tr>
<td>Change on Trails B</td>
<td>0.10</td>
<td>0.010</td>
</tr>
<tr>
<td>Pretreatment COG LAB false</td>
<td>0.20</td>
<td>0.067</td>
</tr>
<tr>
<td>Pretreatment Denman</td>
<td>0.11</td>
<td>0.383</td>
</tr>
<tr>
<td>Nonverbal x treatment dose</td>
<td>0.09</td>
<td>0.486</td>
</tr>
<tr>
<td>Pretreatment NOSIE-30 x treatment dose</td>
<td>0.02</td>
<td>0.904</td>
</tr>
<tr>
<td>Pretreatment Rey VLT visual</td>
<td>0.13</td>
<td>0.214</td>
</tr>
<tr>
<td>form x treatment dose</td>
<td>0.20</td>
<td>0.067</td>
</tr>
</tbody>
</table>

Note.—AIPSS = Assessment of Interpersonal Problem Solving Skills; Trails B = Halstead Reltan Trailmaking B; VLT = Verbal Learning Test; NOSIE = Nurses Observation Scale for Inpatient Evaluation.

1Significance of $T$, reflecting the probability that the variable’s unique contribution to the overall prediction of the dependent variable is zero.

The sizes of most of the interaction terms’ beta weights do not allow confidence that they contribute uniquely to prediction of AIPSS change, but the size for the interaction of cognitive treatment with change on the auditory form of the Rey Verbal Learning Test allows confidence that at least one interaction term is associated with outcome. The Rey VLT is also one of the measures that showed nonspecific improvement (i.e., unrelated to treatment condition) in the outcome study. While learning and memory performance as measured by the Rey improves independently of cognitive treatment, the significant interaction term indicates that the improvement is associated with outcome only if cognitive treatment is provided. This suggests that cognitive therapy works in part by helping patients to use improving learning and memory functioning in situations demanding social competence.

We repeated these analyses using a different outcome variable, a composite measure of performance on four assessments of information acquisition associated with social and living skills training. These consisted of paper-and-pencil quizzes and brief role plays, designed specifically to assess assimilation of information presented in skill training modalities. Such assessments lack the ecological validity of the AIPSS, but they are commonly used to monitor progress in treatment and may reflect more directly patients’ ability to benefit from particular modalities. The path model constructed from measures showing significant bivariate correlations with the skill acquisition change score is shown in figure 2. Unlike the AIPSS model, no pretreatment measures predicted the outcome measure, and cognitive treatment did not affect outcome. Behavioral functioning had a significant impact on outcome, part of which was mediated by reductions in the BPRS disorganization and paranoia dimensions and part by change on the Denman verbal memory score (Denman 1984). The amount of change in paranoia and verbal memory was associated in turn with behavioral functioning as measured by the NOSIE-30. The size of the beta weight of the Denman score is sufficient to allow some confidence that it reflects a real benefit of cognitive change for performance on the skill measure.

Taken together, these analyses suggest that cognitive recovery, especially of verbal learning and memory, has beneficial effects on various aspects of acquisition of social skill and competence in the course of rehabilitation. In some cases, exposure to cognitive treatment may be necessary for patients to fully realize these benefits. However, substantial portions of the improvement in social skill and competence remain unexplained, whether or not the improvement is associated with cognitive treatment. It is hoped that further application of this analytic strategy, with increasingly sophisticated cognitive assessment protocols and with other outcome measures, will identify additional mechanisms and will articulate the importance of additional aspects of cognitive recovery. For the time being, it appears that verbal learning and memory are particularly important targets for treatment.

Possible Mechanisms of the Effects of Psychosocial Interventions in Chronic Schizophrenia

The foregoing results and discussion indicate a need for theoretical models to account for how and why cognitive improvements occur in response to psychosocial treat-
ment in chronic schizophrenia. Discussions of cognitive treatment effects (e.g., Bellack 1992; Corrigan and Storzbach 1993; Brenner et al. 1994; Spaulding et al. 1998; Bellack et al. 1999, this issue) raise the possibility of at least three types of mechanisms: prosthetic mechanisms, in which new skills are established to replace or compensate for impaired abilities; remedial mechanisms, in which the impaired processes undergo actual repair; and reorganizational mechanisms, in which environmental conditions enhance functional reorganization of processes disrupted by acute psychosis. In addition, educational, attributional, and self-instructional mechanisms have been proposed, although these are usually associated with cognitive-behavioral therapy aimed at the content of cognition, independent of neurocognitive impairments (for a review, see Alford and Correia 1994).

Prosthetic, educational, attributional, and self-instructional mechanisms could operate according to familiar models of learning, conditioning, and cognitive development. Remedial mechanisms pose a greater conceptual problem, and it is unclear what kind of model could account for normalization of an otherwise stable neurocognitive impairment. Mechanisms to account for cognitive disorganization and reorganization in schizophrenia have been proposed, in terms of learned behavioral response hierarchies (e.g., Broen and Storms 1966). At least one specific brain mechanism is involved in construction and maintenance of such organizational hierarchies (Houk and Wise 1993; Houk 1995), and it lies in brain structures implicated in the etiology of schizophrenia. Transient physiological dysregulation of such a brain mechanism, as in acute psychosis, could produce a lingering disorganization of response hierarchies, whose reorganization is enhanced by the environmental contingencies and demands associated with psychosocial treatment. Thus, the prospects seem good for credible models to explain prosthetic and reorganizational cognitive treatment effects, especially models that integrate neurophysiological and neuropsychological mechanisms of learning, conditioning, and behavioral organization.

A possible neuroendocrine mechanism of chronic-course cognitive recovery has emerged from studies of
hypothalamic-pituitary-adrenal (HPA) functioning in schizophrenia. The HPA axis has been increasingly implicated in the etiology of schizophrenia, most extensively in Walker and Diforio's (1997) neural diathesis-stress elaboration of Walker's (1994) more general neurodevelopmental model. In this model, prenatal stress leads to high levels of cortisol, causing hippocampal cellular dysplasia. This renders the individual vulnerable to environmental stress by creating a predisposition to HPA axis hyperactivity. HPA hyperactivity continues to interact with hippocampal lesions, leading to further cellular damage. HPA hyperactivity also contributes to expression of psychotic symptoms through activation of subcortical dopamine systems. Cortisol hyperactivity is associated with acute schizophrenia (Albus et al. 1982; Christie et al. 1986; Copolov et al. 1989).

The neural diathesis-stress model describes the HPA's role in onset and acute psychosis, but the model's implications for the chronic course are largely unexplored. HPA activity is affected by antipsychotic drugs. Treatment and rehabilitation environments are usually designed to reduce "stress" and thereby affect HPA activity. Patients' beliefs, attributions, and appraisals about themselves and their control over their environment may undergo dramatic changes after onset, and these factors are known to have significant impact on HPA activity (Lazarus and Folkman 1984). HPA dysregulation can produce a failure of the activating function of cortisol, resulting in a hypoactivation syndrome different in expression from the more familiar hyperactivation/stress syndrome (Chrousos and Gold 1992). It would not be inconsistent with the neural diathesis-stress model to expect that a poorly regulated HPA axis could result in cortisol hypoactivity in the chronic, residual phase of schizophrenia, at least in some patients. In fact, abnormally low levels of cortisol, sometimes to the point of obliterating normal diurnal cycles, have been observed in chronic, stable schizophrenia patients in institutional settings (Bhadrinath and Girijashanker 1984; Spaulding et al. 1990; Partridge 1992; Fleming 1998).

The recent discovery of cortisol receptors in cortical neurons (for a review, see Newcomer et al. 1994) indicates that the activating function of cortisol involves cognitive as well as physiological resources. Experimental suppression of cortisol with dexamethasone in normal subjects is associated with temporary impairments in memory (Newcomer et al. 1994). Cortisol deficiencies produce potentially reversible cognitive deficits in elderly patients (Basavaraju and Phillips 1989).

Of the three studies in our lab that identified institutionalized schizophrenia patients with cortisol hypoactivity, two (Spaulding et al. 1990; Partridge 1992) showed some normalization of cortisol levels and fluctuations associated with intensive psychiatric rehabilitation. The third (Fleming 1998) showed that patients with low cortisol activity also show especially severe impairment in some aspects of cognitive functioning. Taken together, these findings suggest that in the chronic course of schizophrenia, some patients experience a disruption of the regulatory relationship between cognitive and HPA functioning that produces a hypoactivation syndrome. This could be the result of medication, environmental controls, and/or the patient's appraisals and attributions all interacting with an already compromised HPA system. The consequences include residual cognitive impairment. A rehabilitative environment, with systematic and graduated environmental demands for physiological and cognitive activation and attention to the patient's attributions and appraisals, may help reverse this process.

The data showing recovery of cognitive functioning in schizophrenia, and the models that account for that data, suggest a number of conditions that should be expected to maximize recovery. These include environmental engineering that maximizes the clarity and predictability of behavioral performance demands and consequences, psychosocial interventions that exercise key behavioral repertoires and their supporting executive-level cognitive abilities, interventions that address patients' appraisals of stressful events and their control over them, and daily routines that enhance regulatory cycles of organismic activation. Significant cognitive benefits appear to accrue from conventional rehabilitation modalities, including contingency management and skill training, but modalities that specifically target cognitive abilities have added value. However, the heterogeneity of cognitive impairment suggests that individual differences must be taken into account for optimal effect. Despite the overriding role of executive-level cognitive reorganization, different patients rely on different cognitive resources and cope with different cognitive liabilities in the reorganization process. A cognitive technology is needed that is sensitive to such individual differences and allows their consideration in construction of individualized rehabilitation strategies.

Conclusions

Potential applications of cognitive science and technology to schizophrenia go far beyond elucidation of developmental etiological processes. Cognitive functioning is a significant source of individual variation among patients and is importantly related to outcome. Cognitive impairments can change over the acute, post-acute, and chronic course of schizophrenia, in response to psychosocial as well as pharmacological treatment and rehabilitation. The
findings of research using the paradigms of experimental psychopathology and neuropsychology suggest that a cognitive technology can be perfected that would contribute significantly to diagnosis, treatment and rehabilitation planning, evaluation of patients' response to treatment, and the design of future treatment modalities. For some applications, it may be important to revise traditional approaches to behavioral, psychological, and neuropsychological assessment to accommodate the need for longitudinal tracking of recovery over the time frames in which pharmacological and psychosocial treatments exert their effects. Models for systematically applying this technology to clinical assessment and decision making are already beginning to appear (see Spaulding et al. 1994).

To fully realize these potentials, we need research on the cognitive psychopathology and neuropsychology of schizophrenia that systematically addresses the longitudinal course of the disorder, within and across its acute, postacute, and chronic residual phases, in the context of state-of-the-art biopsychosocial treatment and rehabilitation.

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