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A MULTIDIMENSIONAL EXAMINATION OF FUNCTIONAL DISABILITY IN SCHIZOPHRENIA

by

STEFANIE MARA BERNS

A dissertation submitted to the Graduate Faculty in Psychology in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York

1999

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ABSTRACT

A MULTIDIMENSIONAL EXAMINATION OF FUNCTIONAL DISABILITY IN SCHIZOPHRENIA

by

Stefanie Berns

Adviser: Judith Jaeger, Ph.D.

This study aims to elucidate the correlates of the chronic functional disability in schizophrenia by using a multidimensional approach to examine the relative contributions of five domains of neuropsychological functioning (memory, attention, executive, motor and language) and psychopathological symptomatology (including anergia, anxiety, thought disturbance, activation and hostility) to functional disability (including vocational, social, and residential impairment).

Schizophrenia is the most disabling of all psychiatric disorders and the fifth most disabling of all medical disorders in the developed world. Remarkably, the causes of this chronic and pervasive disability are poorly understood and traditional rehabilitation programs and pharmacological treatments have been only minimally successful in improving functional disability. While psychopathological symptoms such as delusions and hallucinations are the target of pharmacotherapeutic and rehabilitation efforts, only a modest relationship between these symptoms and functional disability has been demonstrated. Several recent studies have demonstrated an association between neuropsychological impairment and functional disability that may be independent of psychopathology.

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Sixty outpatients with schizophrenia, age 18 to 45, were administered a set of neuropsychological assessments, psychopathology ratings, and functional disability measures. Canonical correlation analyses revealed that measures of neuropsychological impairment (particularly in the attention domain) were modestly related to one aspect of functional disability, namely, vocational disability. The relationship between psychopathology ratings (particularly anergia and thought disturbance factors) and a different aspect of functional disability, namely social disability ratings reached the level of statistical trend. Analyses of the relationship between current neuropsychological performance, psychopathology ratings, and history of functional disability showed that executive functioning and psychopathology ratings were each related to different aspects of past functional disability. No relationship was found between neuropsychological performance and psychopathology ratings. The findings suggest that neuropsychological functioning and psychopathology reflect modest but independent contributors to functional disability. Increased understanding of the determinants of disability may lead to improvements in pharmacologic, rehabilitative and supportive interventions.

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A MULTIDIMENSIONAL EXAMINATION OF FUNCTIONAL DISABILITY IN SCHIZOPHRENIA

The purpose of this study was to improve the understanding of the determinants of functional disability in schizophrenia. Schizophrenia is the fifth leading cause of disability among all medical disorders in established market economies and is responsible for more years of life lived with disability than all malignancies and HIV combined (Murray & Lopez, 1996). This disability is manifested by a reduction of functional disability (FD) across all realms of life. People with schizophrenia have difficulty with most major aspects of FD such as trouble getting and keeping a job, maintaining a household, managing their finances, and sustaining family relations, friendships and community ties (Anthony, Cohen, and Farkas, 1990). These problems endure in spite of the best available treatment and often persist throughout the person's lifetime (Lehman, Carpenter, Goldman, and Steinwachs, 1995). It has been estimated that impairments in FD exact a financial cost to society 3 to 4 times that of direct patient care (Andrews et al., 1985; Hall et al., 1985). What causes this disability is largely unknown with studies finding only modest relationships between the traditional psychopathological symptoms of schizophrenia (such as hallucinations, delusions, and avolition) and FD (Anthony, Rogers, Cohen, and Davies, 1995; Carpenter & Strauss, 1991). Several recent studies have suggested that neuropsychological (NP) deficits (e.g. impaired memory, attention, executive, motor and language) may be robust contributors to FD (Bilder, 1997; Green, 1996). These studies seeking to determine correlates of functional disability have several limitations including: inadequate measurement of FD, inadequate neuropsychological assessment, small sample sizes, sample selection problems in which the range of levels of

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FD is too restricted to permit proper study, and utilization of a unidimensional approach (ie. examining one aspect of FD or one contributor) (Green, 1996; Liberman, 1997).

The present study attempted to improve upon the methodology used by previous studies to examine the determinants of disability in schizophrenia. A multidimensional approach was utilized to examine the relationships among five domains of NP functioning (memory, attention, executive, motor and language), psychopathological symptomatology (including anergia, anxiety, thought disturbance, activation and hostility) and types of functional disability (including vocational, social, and residential) in a large sample of outpatients. It was hypothesized that NP impairment represented a significant and independent contributor to FD. Identification of the specific correlates of different types of functional disability would provide a guide for the development of more effective interventions for improving the functional disability experienced by individuals with schizophrenia.

DIAGNOSIS AND PSYCHOPATHOLOGY OF SCHIZOPHRENIA

Schizophrenia (SZ) is a chronic psychiatric disorder characterized by a disruption of cognition, emotion, affect, behavior and community functioning. The diagnosis of schizophrenia has changed dramatically over time (Andreasen, 1997). Kraepelin (1919/1971) first identified this disorder as "dementia praecox", an irreversible deteriorating illness stemming from neuropathological disease. Bleuler coined the term "schizophrenia" and broadened the concept to include a group of disorders that all had a "splitting" of psychic functions (Wing, 1995). Schneider narrowed the concept again focusing on 11 "first rank" symptoms that he considered pathognomonic signs of SZ (Andreasen, 1987). The concept of SZ changed again with Freud's influence. Psychoanalytic theory defined SZ as a manifestation of weak ego, an inability to cope

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with life problems with regression to primitive psychosexual level of functioning (Carson & Sanislow, 1993). Recently, findings from genetic and neuroimaging studies have convincingly supported the hypothesis that SZ has an underlying neuropathological basis.

This evolution of the concept of SZ has had tremendous implications. Research has been stymied by the extreme heterogeneity of patients diagnosed with schizophrenia (Jablensky, 1997). This was clearly demonstrated by the landmark US-UK Diagnostic Study (Cooper, 1972) that revealed that the diagnosis of SZ differed tremendously between the United States and the United Kingdom. This led to the development of diagnostic systems to enhance the agreement between clinicians such as the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) (American Psychiatric Association, 1980), Research and Diagnostic Criteria (RDC) (Spitzer, Endicott, and Robins, 1978), and Schedule for Affective Disorders and Schizophrenia (SADS) (Endicott & Spitzer, 1978). These systems are based on consensual criteria and are therefore more objective and less ambiguous allowing for much better interrater reliability. However, they also are somewhat arbitrary and tend to oversimplify the clinical picture (Andreasen, 1997). The diagnostic classification can still include different diseases or disorders with different etiologies that have a similar clinical picture or different diseases that have different clinical pictures.

The current standard for diagnosing schizophrenia is the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (American Psychiatric Association, 1994). The criteria specify that two or more characteristic symptoms (delusions, hallucinations, disorganized speech, disorganized or catatonic behavior, alogia, avolition, or affective flattening) must be present for a significant portion of one month (or for a shorter time if

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responsive to treatment) with continuous signs of disturbance for 6 months. These signs and symptoms must be associated with social or occupational dysfunction and must not be better accounted for by the direct physiological effects of a substance or general medical condition or other psychiatric disorder.

Due to the variability in symptom expression and course of illness, there have been a number of attempts at categorizing patients into more homogenous groups (i.e. negative symptom/positive symptom, reactive/process, paranoid/hebephrenic, Crow's Type I/Type II distinctions, Philip's good premorbid/bad premorbid) (Andreasen, 1982; Crow, 1980a; Langfeldt, 1956; Leonhard, 1980; Tsuang & Winokur, 1974). The DSM-IV recognizes five subtypes of schizophrenia: disorganized, catatonic, paranoid, undifferentiated, and residual. The most studied classification scheme has been positive symptom and negative symptom groups (Andreasen, 1982; Crow, 1980b). Positive symptoms refer to characteristics that are abnormal by their presence (such as hallucinations and delusions) while negative symptoms are abnormal by their absence (including alogia, anhedonia, avolition and flattening of affect). The positive subtype has a more acute onset, better premorbid functioning, and better treatment response and outcome. The negative subtype has been correlated with increased structural abnormalities, poor NP functioning, earlier age of onset, poor premorbid adjustment and poor response to treatment (Andreasen, Flaum, Swayze, Tyrrell, and Arndt, 1990).

Several researchers suggest the two-syndrome model is incomplete and propose a three-factor model comprised of positive, negative and disorganized dimensions (formal thought disorder, inappropriate affect and bizarre behavior) (Bilder, Mukherjee, Rieder, and Pandurangi, 1985; Buchanan et al., 1994; Liddle, 1987). The validity and reliability

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of subtyping schemes have been questioned (Andreasen, 1985). Studies investigating the stability of subtypes over time have been disappointing with stability being the exception not the rule (Deister & Marneros, 1993; Marneros, Rohde, and Deister, 1995). Some argue that studies should classify symptoms and not patients as most patients exhibit a variety of symptoms both positive and negative at any given time and different symptoms over the course of their illness (Frith, 1992). The extent of the heterogeneity has called into question the validity of the definition as a single disease and has led to the reexamination of the possibility that SZ is comprised of several different disorders (Carson & Sanislow, 1993; Jablensky, 1997).

In summary, the search for a definition of schizophrenia has been a fundamental question that has plagued researchers for the past century.

EPIDEMIOLOGY OF SCHIZOPHRENIA

Hare (1987) presents epidemiologic data based on a review of many studies and finds that schizophrenia has a lifetime prevalence rate of approximately one percent, a point prevalence rate of 2%, and an incidence rate of 30 per 100,000 per year.

Although there is no gender difference in the incidence or prevalence of schizophrenia, men are more likely than women to have an earlier onset (median age is in the early to mid twenties), poor premorbid adjustment, less education, more structural brain abnormalities, more negative symptoms, worse response to medication, more NP impairment, and poorer course and outcome. Women have a later onset (median age is in the late twenties), better premorbid and occupational history, more mood symptoms, and a better prognosis (Goldstein, 1996).

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The financial cost of schizophrenia is tremendous. As the illness often begins in early adulthood and is associated with a chronic and disabling course, the indirect costs through loss of productivity are 3 to 4 times that of direct patient care (Andrews et al., 1985; Fein, 1958; Gunderson & Mosher, 1975; Hall et al., 1985). Wyatt et al. (1995) reported that in 1991, the total annual cost of schizophrenia in the United States, including was 65 billion dollars with direct costs totaling $19 billion and indirect costs of $46 billion. Schizophrenia accounts for 2.5% of the total health care expenditures in the US although it affects only 1% of the population (Rupp & Keith, 1993).

There is a lack of agreement in the literature about the course and outcome of the illness. Some followup studies reveal a predominantly deteriorating course with poor outcomes (Breier, Schreiber, Dyer, and Pickar, 1991; McGlashan, 1986) while others find a majority improving over time (Ciompi, 1980; Harding, Brooks, Ashikaga, Strauss, and Breier, 1987). Most studies demonstrate significant heterogeneity in course and outcome (Carpenter & Strauss, 1991; Huber, Gross, Schüttler, and Linz, 1980). Better prognosis has been associated with being female, precipitating events, an associated mood disturbance, a brief duration of active phase, good inter-episode functioning, minimal residual symptoms, absence of structural brain abnormalities, normal neurological function, family history of mood disorder, and no family history of schizophrenia (American Psychiatric Association, 1994; Kay & Lindenmayer, 1987b). This variability may be due to the use of different diagnostic criteria, sampling of patients, length of followup, and measurement of outcome (Marengo, 1994). Breier et al. (1992) reviewed this literature and proposed a model of the course of illness through the life span that consisted of three phases: an early phase of deterioration from premorbid levels of

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functioning, a middle phase characterized by stabilization and a later phase of improvement in functioning. The life expectancy of individuals with schizophrenia is reduced (Allebeck, 1989) and the suicide rate is increased relative to the normal population (Ciompi, 1980).

Etiology is still unknown. Genetic theories are supported by the fact that concordance rates are higher in monozygotic twins (31 to 78%) than in dizogotic twins (0-28%) (Kendler & Diehl, 1993; Schulz, 1991). However, the lack of complete concordance in monozygotic twins suggests that non-genetic factors also play a part. First degree relatives of individuals with schizophrenia have an increased risk of manifesting SZ (3-7%) when compared to first degree relatives of control subjects (.5-1%) even if raised by adoptive parents (Kendler & Diehl, 1993).

FUNCTIONAL DISABILITY IN SCHIZOPHRENIA

Schizophrenia is the fifth leading cause of disability among all medical disorders in established market economies and is responsible for more years of life lived with disability than all malignancies and HIV combined (Murray & Lopez, 1996). It is the most disabling of all psychiatric disorders (Harrow, Sands, Silverstein, and Goldberg, 1997; Moller, Schmid B.W., Cording T.C., Wittchen, and et al, 1988). Individuals with schizophrenia have significant impairments across vocational, educational, social, and residential domains.

Vocational Disability

Recent large scale followup studies have reported that the majority of patients with schizophrenia demonstrate poor vocational functioning (Breier et al., 1991; Harding et al., 1987; Harrow et al., 1997; McGlashan, 1986; Moller et al., 1988). McGlashan

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(1986) reported that 51% of the sample of 163 patients with schizophrenia from the Chestnut Lodge followup study were never employed in any capacity during the followup period that averaged 15 years. Using census data, Aro et al. (1995) demonstrated that individuals with schizophrenia (in comparison to the general population and their parents) function at vocational levels below expectations with a progressive downward drift often to unemployment. First episode patients have a high rate of unemployment which has been shown to increase over time (Beiser et al., 1994). Vocational rehabilitation programs have been minimally effective in improving competitive employment rates (Becker & Drake, 1994). Placement rates have been shown to be as low as 15-30% with only half of the patients able to maintain employment for more than six months (Anderson, Reiss, and Hogarty, 1986). It has become apparent that the greatest challenge lies in sustaining employment. Supported employment programs have received a great deal of interest recently underscoring the need for ongoing support to sustain improvements in vocational functioning (Gervey & Bedell, 1994; Torrey, Becker, and Drake, 1995; Trotter, Minkoff, Harrison, and Hoops, 1988).

Educational Disability

Individuals with SZ also demonstrate reduced achievement in school. IQ scores of children who later were diagnosed with SZ were compared to citywide averages and with normal controls consisting of their classmates, siblings, and neighbors. The SZ group had significantly lower scores in grades 2, 6 and 8 than their peers (Albee, Lane, and Reuter, 1964). A similar study found the children who became adults with SZ had significantly lower IQs in the 2nd grade than their siblings who were tested when they were in the 2nd grade with the same tests (Lane & Albee, 1964). Jones et al. (1994)

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demonstrated that low educational test scores at ages 8, 11, and 15 years were a risk factor for developing schizophrenia in a large epidemiological study that followed all children born in England in one week in 1946 for 40 years.

Supported education programs have become more widespread reflecting the need for assistance in this domain (MacDonald-Wilson, Revell, Hguyen, and Peterson, 1991).

Social Disability

Impairment in social functioning is also a devastating feature of SZ that pervades all stages of the illness. Individuals with schizophrenia show deteriorating social functioning such as poor social involvement with friends and relatives and increased isolation even predating the onset of illness (Mueser, Bellack, Morrison, and Wixted, 1990). Reduced premorbid social competence has been shown to be predictive of the development of schizophrenia as well as the course and outcome of the illness including increased relapse, poor social skills, poor quality of interpersonal relationships and poor community adjustment (Strauss & Carpenter, 1977). Celibacy rates are significantly higher in individuals with SZ and the number of children produced is significantly lower than that of the general population (Rosenthal, 1970). Social deficits have been found to be related to increased relapse rates, overall poor outcome, and lower quality of life reported by SZ patients (Perlick, Stastny, Mattis, and Teresi, 1992c). While the high prevalence and functional significance of social functioning impairment is undisputed, little is known about what factors contribute to the impairment. SZ patients display many impairments in their interpersonal behaviors including, increased latency, reduced content and duration of verbal response, decreased use of gestures, and abnormal gaze pattern (Bellack, Sayers, Mueser, and Bennett, 1994). Deficits in social perception are

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also common including decoding of facial and vocal expressions. These deficits are more severe than those seen with other diagnostic groups (Bellack, Morrison, Mueser, Wade, and Sayers, 1990a). Social skills training programs have been developed to help ameliorate these impairments with some evidence of improvement in social skills and outcome (Mueser, Bellack, Douglas, and Morrison, 1991a). However, these patients have difficulties maintaining their gains over time and generalizing to novel situations.

Residential Disability

Deinstitutionalization has increased the number of people with SZ living in the community and decreased the amount of time patients with SZ are hospitalized; however, these results do not reflect the ongoing impairments in independent living (Stein & Test, 1980). Most people with SZ require supervised living arrangements and are dependent on social services for money, food and shelter. Many live with their parents who support them both financially as well as practically by taking over their residential responsibilities (cooking, cleaning, budgeting, etc.). People with SZ may also be placed in supportive housing programs that attempt to phase out supports beginning with constant care environments such as adult homes, to group homes where the patient has some responsibilities, to apartments where staff only visit occasionally. This model assumes that patients will continue to improve in their ability to live independently, however, this does not always occur. Some people with SZ live in substandard housing, in shelters or are homeless (Bellack & Mueser, 1986; Carling, 1995; Gourovitch, Goldberg, and Weinberger, 1997).

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Summary

The disability individuals with schizophrenia face may be best voiced by a first person account (Herrig, 1995): "Nine years have passed since I was hospitalized. . . . These 9 years have been filled with many disappointments. I've gone through long periods of unemployment. At 31 I am single and unable to support myself. I live with my parents."

Individuals with SZ demonstrate significant disability across all domains of independent functioning (vocational, educational, social and residential). Traditional models of psychiatric rehabilitation have been shown to be only partially successful at improving functional disability in the vocational, educational and social domains. The most successful rehabilitation approaches have been those that provide individualized ongoing support. This suggests that enduring impairments underlie functional disability and that rehabilitation approaches are not addressing the fundamental problem.

PATHOPHYSIOLOGY OF SCHIZOPHRENIA

Almost a century ago, Kraepelin wrote of dementia praecox (1919/1971 p. 219), "If it should be confirmed that the disease attacks by preference the frontal areas of the brain, the central convolutions and the temporal lobes, this distribution would in a certain measure agree with our present views about the site of the psychic mechanisms which are principally injured by the disease."

The advance of psychodynamic theories as well as early failures to locate the identifying lesion led to a shift away from brain-based theories of the etiology of schizophrenia (Chua & McKenna, 1995). Recent findings from neuroimaging studies have revived interest in schizophrenia as a neuropsychiatric disease. Evidence from in

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vivo imaging techniques of computed tomography (CT) and magnetic resonance imaging (MRI) have firmly established the presence of structural brain abnormalities in schizophrenia (Falkai & Bogerts, 1995). Similarly, functional brain abnormalities have been discovered through the use of regional cerebral blood flow (rCBF), positron-emission tomography (PET), single photon emission computed tomography (SPECT) and functional magnetic resonance imaging (fMRI). The most consistent findings are summarized below.

A recent review of 40 MRI studies that reported volumes of cortical structures in individuals with schizophrenia and controls revealed that several brain structures are affected to a greater extent than expected from overall reductions in brain volume. Median percentage volume differences revealed a 3% reduced whole brain volume, increases in the lateral ventricles (44% left, 36% right), and reductions in the temporal lobe (6% L, 9.5% R) and amygdala/hippocampus (6.5%L,5.5%R) (Lawrie & Abukmeil, 1998).

Ventriculomegaly

The most consistent finding has been the enlargement of the cerebral ventricular system particularly the lateral and third ventricles. In discordant monozygotic twins, CT and MRI shows the affected twin has larger ventricles even if the ventricles are all within the normal range (Suddath, Christison, Torrey, Casanova, and Weinberger, 1990). Also, first episode, untreated patients with schizophrenia have enlarged ventricles suggesting that these findings are not secondary to pharmacotherapy or to chronicity (Lieberman et al., 1992). Ventricular enlargement appears to be static and non- progressive (Jones & Akbarian, 1995). While some studies demonstrate more significant abnormality in the

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left hemisphere, the finding appears to be bilateral (Hyde, Casanova, Kleinman, and Weinberger, 1991). Ventriculomegaly has been found to be consistently associated with unemployment (Pearlson, Garbacz, Breakey, Ahn, and DePaulo, 1984; van Os et al., 1995) and neuropsychological impairment as well as inconsistently with negative psychopathological symptoms, chronicity of illness, and treatment response (Chua & McKenna, 1995). Thus, ventricular enlargement appears to be a well-established structural abnormality is schizophrenia. However, it is not a finding specific to schizophrenia as it occurs in many other disorders including mood disorders (Syvalahti, 1994).

Temporolimbic structures

Antemortem and postmortem studies have revealed reduced tissue volume and neuroanatomical anomalies in the temporal lobes especially in the amygdala, hippocampus and parahippocampal regions (Bogerts & Falkai, 1991; Chua & McKenna, 1995; Hyde et al., 1991; Lawrie & Abukmeil, 1998; Syvalahti, 1994; Szymanski, Kane, and Lieberman, 1991; Tamminga, 1997). PET studies have shown lower metabolic rates in the left temporal lobe region (Tamminga et al., 1992). MRI studies in discordant monozygotic twins reveal bilateral reduction of the anterior hippocampus and loss of grey matter in the left temporal lobe in the affected twin, however, this could be due to the neuroleptics taken by the SZ twins (Suddath et al., 1990). Reduced hippocampus size is also seen in first episode patients (Bilder et al., 1995). Histological studies show disturbed cortical lamination patterns and disarray of the dendritic arborizations in the hippocampus and parahippocampal regions interpreted as resulting from defective neuronal migration (Jones & Akbarian, 1995). This suggests that the neuropathological

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basis of the volume reduction may stem from a developmental defect. Although some data suggest the left hemisphere pathology is more robust, bilateral findings are the rule not the exception (Hyde et al., 1991).

Prefrontal Cortex

Reduced blood flow to the prefrontal cortex (hypofrontality) has been inconsistently reported. A recent review of 27 studies reported that only 10 had evidence of statistically significant hypofrontality (measured while the subject is at rest). However, when the subjects are imaged while being administered an executive functioning task, hypofrontality is seen more consistently (Weinberger, Berman, and Zec, 1986). Studies of monozygotic twins discordant for SZ reveal no evidence of hypofrontality in unaffected twins while hypofrontality was seen during the WCST test in every affected twin tested (Berman & Weinberger, 1991). Hypofrontality does not seem to be due to neuroleptic treatment as it is seen in first episode patients never exposed to neuroleptic treatment (Andreasen et al., 1992). There is evidence that hypofrontality is related to negative symptoms (Chua & McKenna, 1995).

Cerebral Asymmetry

Asymmetries between the left and right hemispheres of the brain are normally seen. In most people, the right frontal lobe is larger than the left, the left occipital lobe is larger than the right, and the left planum temporale (underlying the sylvian fissure) is larger than the right. These asymmetries are a recent evolutionary development and language is believed to have evolved through the expansion of the left temporal lobe. Studies of cerebral asymmetries in patients with SZ have revealed reversals and reductions but not consistently. However, this is not specific to SZ and not all patients with SZ show

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abnormal asymmetry. The functional significance of these abnormalities also remains unclear (DeLisi et al., 1997).

Associated Neurological Findings

Impaired Sensory Gating

Individuals with schizophrenia may have impairments in underlying neural systems as evidenced by a lack of pre-pulse inhibition of the startle response. This is a diminution of a normal protective, preattentive "gating" that suggests that SZ patients have deficient inhibitory functions that may translate into a vulnerability to sensory overload (Szymanski et al., 1991).

Eye Movement Dysfunction (EMD)

Patients with schizophrenia have less accurate smooth pursuit eye movements (deviation of eye position from the pattern made by a target) and make more frequent saccades than normal controls. EMD is found in 50-80% of individuals with SZ as well as in 45% of close relatives but only 5-8% of the normal population (Syvalahti, 1994; Szymanski et al., 1991). EMDs are not induced by or improved with neuroleptic medication and they are independent of changes in clinical state. EMD has been described as a biological marker for schizophrenia, however, it is not specific to schizophrenia.

Abnormalities of Event Related Potentials (ERP)

A reduction in the amplitude and an increase in the latency of the P300 brain potentials (generated when infrequently occurring sensory stimuli are detected or when unexpected and highly unusual stimuli are delivered) are seen in patients with SZ. This is

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thought to reflect abnormalities of the medial temporal lobe limbic structures and has been shown to correlate with attentional deficits (Szymanski et al., 1991).

Gender and Pathophysiology

While the findings are inconsistent, studies analyzing gender differences in structural brain abnormalities in SZ have suggested that men have more such pathology than women (Goldstein, 1996). Greater ventricular enlargement (Flaum, Arndt, and Andreasen, 1990; Haas, Sweeney, Hein, Goldman, and Deck, 1991), increased sulcul volume (Gur et al., 1991) and decreased thalamic, frontal and temporal lobe volumes (Bogerts et al., 1990) have been reported in SZ men. These structural abnormalities occur more frequently in the left hemisphere in men (Hoff et al., 1992).

Summary

Overall, there is good evidence that the brain is structurally and functionally abnormal in schizophrenia (Tamminga, 1997). Diminished volume of brain regions and increased ventricular size are widely accepted correlates of SZ (Lawrie & Abukmeil, 1998). However, the degree of change is small and these changes are nonspecific to schizophrenia occurring in a number of disorders. While there have been many exciting findings there is still no conclusive candidate for an underlying causal pathology of schizophrenia. The low replication of findings may be due to the considerable variability in methodology, the inherent heterogeneity of SZ patients as well as the small magnitude of change in schizophrenia (Chua & McKenna, 1995). Buchanan and Carpenter (1997) argue that the search for the pathophysiology of SZ has not addressed the heterogeneity of schizophrenia and propose that future studies should associate neuroanatomical

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measures with "independent symptom complexes" such as positive and negative symptoms.

NEUROPSYCHOLOGICAL IMPAIRMENT IN SCHIZOPHRENIA

Neuropsychological impairment in schizophrenia has been recognized for almost a century. Despite the continual changes in the diagnostic criteria, treatments available and testing paradigms since the beginning of the century, the finding that SZ patients perform more poorly on a wide range of cognitive tasks than do normal controls has remained consistent. NP impairment is increasingly regarded as behavioral evidence of the neuropathology underlying SZ (Gold & Harvey, 1993; Gold & Weinberger, 1995). The literature review following describes the impairment seen in SZ for the five domains of neuropsychological functioning that are assessed in this study (attention, memory, executive functions, motor, and language).

Domains of Neuropsychological Impairment

Attention

Individuals with schizophrenia perform poorly on a number of attention paradigms in both auditory and visual modalities (Randolph, Goldberg, and Weinberger, 1998). Deficits in simple attention functions are seen in an unusually slow and variable reaction time (even after motor slowing is accounted for). Difficulty with selective attention is demonstrated by impaired performance on dichotic listening tasks or visual tasks that require the patient to selectively attend to relevant information while ignoring unimportant information (Gold & Harvey, 1993). Deficits in the alerting, shifting, and response preparation aspects of attention are suggested by their inability to benefit from regular preparatory or warning intervals, as well as the poor use of cues to facilitate their

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performance. People with schizophrenia also do poorly on tasks assessing vigilance (the ability to sustain attention over time) making an abnormally high number of omission errors even in simple versions of continuous performance (CPT) tasks (Gold & Harvey, 1993; Goldberg, Gold, and Braff, 1991; Randolph et al., 1998)

Memory

Impaired performance is seen in patients with schizophrenia using a variety of paradigms implicating all stages of memory function. Deficits have been demonstrated in the encoding, consolidation, retrieval and recognition of both visual and verbal material (Gold & Harvey, 1993; Goldberg et al., 1991). Goldberg et al. (1990) found that in discordant monozygotic twins, the affected twin performed an average of 23 points lower on the Wechsler Memory Scale-Revised (WMS-R) (Wechsler, 1987) than the unaffected twin. Gold et al. (1992) reported that the majority of the SZ sample performed relatively lower on the WMS-R than on the Wechsler Adult Intelligence Scale-Revised (WAIS-R) (Wechsler, 1981). This memory-intelligence discrepancy suggests differential memory impairment. This study also reported evidence that the memory deficits are not secondary to attentional impairment. Patients with a large intelligence-memory discrepancy were compared with patients with a small discrepancy and there was no significant difference in their performance on attention measures. Also, SZ patients' performance on memory tests does not correlate with the attentional demands of the tests. They perform poorly on memory tasks that are considered to be relatively automatic and free of an attentional load such as estimating the frequency of occurrence of recent events (Gold & Harvey, 1993). The finding of significant memory impairment in SZ is consistent with the structural and functional abnormalities found in

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the medial temporal lobes (Lawrie & Abukmeil, 1998; Syvalahti, 1994; Tamminga et al., 1992), as mentioned previously, as this area plays a crucial role in mnemonic functioning.

Executive Functions

A striking feature of schizophrenia is the similarity in behavior with patients having frontal lobe disease. These two groups display poor social judgement, planning ability, and insight as well as aspontaneity, anhedonia and affective flattening (Randolph et al., 1998). Patients with schizophrenia show impaired performance on NP tests sensitive to frontal lobe dysfunction. They have difficulty with tasks that involve problem solving, concept formation, set shifting and response to feedback often perseverating on incorrect responses in the face of feedback to the contrary (Goldberg et al., 1991). The tenacity of the deficit was revealed by Goldberg et al. (1987b) who demonstrated that the deficit remained even after explicit instruction on how to complete the Wisconsin Card Sorting Test (WCST). Several studies have shown that patients with schizophrenia have reduced blood flow in the dorsolateral prefrontal cortex during the WCST (Berman, Zec, and Weinberger, 1986; Weinberger & Berman, 1988; Weinberger et al., 1986). This was not observed by these authors with other tasks or in other cortical areas.

Motor

Patients with schizophrenia often display disturbances in voluntary and involuntary motor control including incoordination, clumsiness, tremors and posturing (Manschreck, 1983). These patients show significant impairments on simple motor tasks such as finger tapping and manual dexterity bilaterally. Motor abilities decrease as task complexity increases. Psychomotor slowing (such as reduced reaction time) is

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consistently found but this motor behavior is often confounded by attentional variables (Levin, Yurgelun Todd, and Craft, 1989). SZ patients display more neuromotor abnormalities than patients with other psychiatric disorders as well as normal controls (Walker & Green, 1982). This motor dysfunction is evident very early in life. Walker et al. (Walker, Savoie, and Davis, 1994) reported evidence of motor disturbance as early as in the first two years of life from the study of home movies of pre-SZ patients and their well siblings during the first years of life. Jones et al. (1994) in a large epidemiological study that followed all children born in England in one week in 1946 for 40 years, demonstrated that milestones of motor development, particularly walking, were reached later in the 30 children who developed SZ than in those who didn't develop SZ. While motor disturbances are a common side effect of antipsychotic medication, impairments were also described in the pre-neuroleptic era (Kraepelin,1919/1971).

Language

Patients with schizophrenia display expressive speech abnormalities. Linguistic studies have demonstrated impairments in semantic content, discourse and complexity (Levin et al., 1989). Language comprehension deficits are also seen in patients with SZ as are dysfunctions in pragmatics (use of language in a social context) (Condray, van Steinhauer, Kasparek, and Yao, 1995). Language impairment is seen in first episode patients as well as in children who were later diagnosed with SZ (Baltaxe & Simmons, 1995). Syntactic complexity has been shown to be related to age of onset and time since onset (Thomas et al., 1995). These findings are consistent with neuropathological abnormalities of the left temporal lobe.

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Prevalence of Neuropsychological Impairment

Prevalence has been studied by applying cutoff scores derived from NP comparisons of brain-damaged to normal and psychiatric. However, this approach suffers from the problem of what is "normal" cognitive performance for any given individual. The crucial comparison may not be how a person with SZ performs relative to the normal population but relative to expectations had the disorder not developed. Goldberg et al. (1990) reported findings from their study of discordant monozygotic twins that more than 80% of the affected twins performed worse than their unaffected co-twin on measures of intelligence, memory, attention, and executive functioning. This was true even when the performance of the affected twin was considered to be within normal limits. Thus, individuals with SZ tend not to reach their cognitive potential. Also, some degree of NP impairment is seen in nearly all cases and there does not appear to be a subgroup of patients who demonstrate intact NP functions.

Course of Neuropsychological Impairment

Retrospective studies of IQ and academic performance suggest that a significant number of children who later developed schizophrenia exhibited deficits in comparison to siblings and peers (Penn, 1991). High risk studies reveal attentional abnormalities in children of patients with schizophrenia. Early attentional impairment has been shown to be predictive of later development of serious psychiatric illness (Cornblatt & Keilp, 1994). These findings suggest that subtle NP dysfunction is often present well before the onset of overt psychotic symptoms. First episode studies clearly demonstrate that NP impairments present at the onset of psychosis (Bilder et al., 1992). Saykin et al. (1994) demonstrated that first episode patients had nearly identical profiles of generalized

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neuropsychological impairment when compared with previously treated patients. Some short-term followup studies have indicated some improvement in NP functioning following an acute episode (Smet et al., 1995; Sweeney, Haas, Keilp, and Long, 1991). However, longitudinal studies and studies comparing first episode patients with chronic patients suggest that the deficits are relatively stable over time with evidence that they are unrelated to current age, age of onset or duration of illness (Harrow, Marengo, Pogue-Geile, and Pawelski, 1987; Heaton, Paulsen, McAdams, Kuck, Zisook, Braff, Harris, and Jeste, 1994; Hoff, Riordan, O'Donnell, and Morris, 1992). Heaton and Drexler's (1987) review of 100 cross-sectional studies that contained neuropsychological data from patients in various age groups provide strong support for the stability of NP impairment. These lines of evidence support the idea that NP impairment reflects a trait, rather than a state dependent, characteristic in schizophrenia.

Severity of Neuropsychological Impairment

NP studies have shown that SZ patients perform at levels that closely resemble that of patients with diffuse brain injury. It is often impossible to discriminate between these two groups of patients on NP tests alone. NP deficits are more severe in schizophrenia than those seen in any other psychiatric illnesses. Overall, cognitive performance is generally at the level of mild to moderate impairment (1 to 2 standard deviations below normal controls), IQ scores are one half to one SD below the population mean and problem solving deficits approach the level of patients with coarse frontal lobe damage (Goldberg et al., 1991).

Another way to determine the severity of NP deficits in SZ is to compare these patients with patients with developmental neurological conditions. Gold et al. (1994)

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compared SZ patients (N=66) with patients with intractable frontal or temporal lobe epilepsy (N=101) and found these two groups had the same degree of impairment.

Pattern of Neuropsychological Impairment

There is also no general agreement as to whether these deficits indicate a global impairment or selective impairment obscured by the heterogeneity of the population. As a group, patients with schizophrenia perform significantly more poorly than normal controls across all neuropsychological domains. However, these studies also report a high degree of within subject variation. Differences in NP test difficulty, standardization and psychometric properties make comparisons of the relative impairment between tests unwise (Chapman & Chapman, 1973). For example, patients may do worse on test A than test B but that difference in performance may be due to test A being more difficult than test B. Without psychometrically matched neuropsychological tests, findings of differential impairment are questionable.

Given this qualification, several authors have reported evidence of selective impairment superimposed on a generalized impairment. Saykin et al. (1991) administered a comprehensive neuropsychological battery to 36 medication free patients with schizophrenia and 36 age-matched normal controls. Patients scored lower than controls across all NP functions tested (abstraction, verbal cognitive, spatial organization, semantic memory, visual memory, verbal learning, language, visual-motor processing, auditory processing and attention, and motor speed and sequencing). However, the profile was not flat and there was a significant function by diagnosis interaction. Comparisons between the functional domains revealed even greater impairment in memory and learning functions than others assessed. Saykin et al. (1994) replicated this

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finding in another study using the same methods to compare a sample of 37 patients in their first episode of schizophrenia who had never been medicated with 65 currently unmedicated but previously treated patients as well as 131 healthy controls. Both patient groups performed significantly below the healthy controls. The previously treated group performed significantly lower than the first episode group. However, no difference was found in profile shape as both showed an increased impairment in verbal memory and learning in comparison with other NP functions. Flashman et al. (1995) report on a study that also suggests that the neuropsychological impairment seen in schizophrenia can be best described as having specific deficits superimposed on a generalized impairment. A comprehensive battery of neuropsychological measures was administered to134 patients with schizophrenia and 193 normal controls. The schizophrenic group was significantly more impaired on all measures but when IQ was statistically controlled, the schizophrenic patients displayed a selective impairment in verbal memory and perceptuomotor speed.

Heinrichs & Zakzanis (1998) completed a meta-analysis of 204 studies that had neuropsychological performance data on both normal controls and SZ patients. The results suggest that all areas of NP functioning are impaired to at least a moderate degree in a large proportion of patients with SZ. The authors report variability in the magnitude of deficit with the largest effect sizes from global verbal memory, performance and full scale WAIS-R IQ, attention and verbal fluency while the smallest effect sizes stemmed from WAIS-R Block Design and Vocabulary subtests.

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Gender and Neuropsychological Impairment

The literature has been inconsistent with regard to gender differences in neuropsychological performance in schizophrenia. Some studies report males perform worse on NP tests than females in a variety of domains including intelligence, attention, memory, motor, language and executive functioning (Goldstein, Seidman, Santangelo, Knapp, and Tsuang, 1994; Haas et al., 1991; Seidman et al., 1997) while some find no difference between genders (Goldberg, Gold, Torrey, and Weinberger, 1995; Hoff et al., 1992) and others find greater impairment in women on tests of memory and visual processing (Lewine, Walker, Shurett, Caudle, and Haden, 1996). The inconsistency may be due to methodological differences such as different sampling strategies and sample sizes (Goldstein, 1996). Haas et al. (1991) report that a first-episode group of SZ patients (N=63) showed no differences in neuropsychological performance while a group of more chronic patients (N=93) revealed a gender difference such that males performed significantly worse than females on memory, verbal fluency, attention and motor tasks. Goldstein et al. (1998) report on a study designed specifically to test for gender differences in neuropsychological performance that included 31 outpatients with schizophrenia sampled from an extensive urban catchment area and 27 normal comparison subjects matched within sex. When compared with the matched normal controls, male patients were significantly impaired across all domains while female patients performed worse only on tests of attention, executive functions, visual memory and motor tasks. Male patients performed worse than did female patients on tests of attention, verbal memory and executive functions. These findings suggest that women with schizophrenia exhibit fewer and less severe neuropsychological deficits (particularly

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those involving verbal processing) than men. This is consistent with the studies that report that men have an earlier age of onset and poorer premorbid history suggesting earlier developmental deficits that may contribute to their neuropsychological performance.

Primary versus Secondary Impairment

It has been suggested that the neuropsychological impairment seen in patients with schizophrenia is secondary to other factors such as neuroleptic medication, institutionalization and psychopathological symptoms. However, studies have shown that these factors do not substantially affect neuropsychological functioning as described below (Randolph et al., 1998). The evidence supports the view that NP deficits are not epiphenomena but are core features of schizophrenia (Weinberger & Gallhofer, 1997).

Neuropsychological Impairment and Long Term Institutionalization.

Studies have consistently failed to find significant effects of hospitalization on neuropsychological impairment. Harrow et al. (1987) found no difference in performance on intelligence and abstract thinking measures between a group of 39 continuously hospitalized patients and a matched group of 38 intermittently hospitalized patients with chronic schizophrenia. Duration of hospitalization did not account for a significant portion of the variance in neuropsychological test performance in a study of 245 schizophrenic patients (Goldstein, Zubin, and Pogue, 1991). Therefore, early concerns that NP impairment was limited to the chronically institutionalized patients appear to be unfounded.

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Neuropsychological Impairment and Psychopathology

Another concern has been that NP deficits might be secondary to psychopathological symptoms. Perhaps the distracting nature of hallucinations and delusions impact the patient's ability to perform well on NP tests. This literature is quite conflicting and is difficult to interpret due to inconsistencies in neuropsychological test protocols, symptom ratings, use of multiple comparisons, and subject selection. However, there is compelling evidence that supports the independence of neuropsychological deficits and psychopathological symptomatology. At risk, first episode and longitudinal studies demonstrate that NP deficits exist prior to the development of symptoms and remain relatively stable in the face of the significant changes seen in psychopathological symptomatology over time (Nopoulos, Flashman, Flaum, and Arndt, 1994).

While a few studies have shown relationships between auditory attention impairment and positive (Berman et al., 1997; Cornblatt, Lenzenweger, Dworkin, and Erlenmeyer-Kimling, 1985; Green & Walker, 1985; Green & Walker, 1986), as well as disorganized symptoms (Bilder et al., 1985; Brekke, Raine, and Thomson, 1995; Liddle et al., 1992), these findings have not been replicated in the vast majority of studies (e.g. Addington, Addington, and Maticka-Tyndale, 1991; Breier et al., 1991; Brekke et al., 1995; Buchanan et al., 1994; Perlick, Mattis, Stastny, and Silverstein, 1992a).

Studies of the relationship between negative symptoms and NP test performance have been inconsistent and where correlations are found, they are modest and only account for a small portion of common variance (Goldberg et al., 1991). Several studies have demonstrated correlations between negative symptoms and executive functioning

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(Addington et al., 1991; Berman et al., 1997; Breier et al., 1991; Capleton, 1996; Perlick et al., 1992a). Some have shown relationships between negative symptoms and verbal memory (Paulsen et al., 1995), visual attention (Nuechterlein, Edell, Norris, and Dawson, 1986), verbal attention (Goldman et al., 1993), and visuomotor and visuospatial processes (Brekke et al., 1995; Brown & White, 1992; Cornblatt et al., 1985; Green & Walker, 1985).

However, many of these studies have an unintended confound in which negative symptom rating scales include items that reflect cognitive processes. The "Attention" items of the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1981) include the "serial 7s" and spelling "world" backward tasks from the Mini Mental State Examination (Folstein, Folstein, and McHugh, 1975). The Positive and Negative Syndrome Scale for Schizophrenia (PANSS) (Kay, Fiszbein, and Opler, 1987a) includes two items that rate neuropsychological functions: "difficulty in abstract thinking" and "poor attention". It even includes tasks similar to the Similarities and Comprehension subtests of the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981) to assist in the ratings. Thus, relationships between negative symptoms and NP performance may be inflated.

Neuropsychological Impairment and Neuroleptic Medication

Reviews of the effect of neuroleptic medication on neuropsychological functioning have consistently suggested that the impact is minimal with only some evidence of psychomotor slowing and slight improvement in attentional functions (Bilder, 1997; Cassens, Inglis, Appelbaum, and Gutheil, 1990; Heaton & Crowley, 1981b; Medalia, Gold, and Merriam, 1988; Spohn & Strauss, 1989). Seidman et al.

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(1993) reported stability of neuropsychological performance despite significant changes in the dosage of neuroleptics. NP deficits seem to be only inconsistent predictors of short term neuroleptic treatment response (Stern, Kahn, and Davidson, 1993). Overall traditional neuroleptics provide little direct benefit or cost to their neuropsychological performance for most patients (King, 1994). This finding that NP deficits are not significantly affected by neuroleptic medication despite significant reduction of psychopathological symptoms is perhaps the most convincing demonstration of the independence of psychopathology and NP impairment.

Newer "atypical" neuroleptics such as clozapine show more promise for improving NP functioning as well as reducing psychopathology. While some studies show little impact on NP performance (Goldberg et al., 1993), others have shown improvement in attention, memory and executive functioning (Hagger et al., 1993; Meltzer, Thompson, Lee, and Ranjan, 1996). Clozapine has a different mechanism of action than typical neuroleptics and has a broader impact on neurotransmitter systems (including not only the dopamine system but also the serotonergic, adrenergic, histaminergic and muscarinic systems). Thus, atypical neuroleptics may affect both psychopathology and NP functioning by its impact on different aspects of brain functioning.

Summary

Studies have consistently found NP impairments in nearly all patients with SZ. Recent neuroimaging and postmortem studies have revealed evidence of abnormalities in the medial temporal lobe structures and a pattern of hypofrontality that is consistent with the NP findings. These deficits are chronic and severe and cannot be fully explained by

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the effects of medication, institutionalization or psychopathology. Neuropsychological deficits are present before psychopathological symptom development, are not significantly ameliorated by neuroleptic treatment and are relatively stable over time.

CORRELATES OF FUNCTIONAL DISABILITY

Psychopathology and Functional Disability

Studies have consistently found little or no correlation between either overall psychopathological symptomatology or positive psychopathological symptoms and functional disability (i.e. Anthony & Jansen, 1984; Bellack et al., 1990a; Bellack, Morrison, Wixted, and Mueser, 1990b; Bellack et al., 1994; Carpenter & Strauss, 1991; Harding et al., 1987; Mueser, Bellack, Douglas, and Wade, 1991b; Strauss & Carpenter, 1972; Strauss & Carpenter, 1978; Strauss, Carpenter, and Bartko, 1974). This well-established finding in the literature continues to surprise and frustrate clinicians as well as patients and their families who anxiously await a return to ordinary life when the symptoms are reduced with pharmacologic treatment.

Some studies have revealed a relationship between negative symptoms and measures of social skills (Bellack, Morrison, Mueser, and Wade, 1989; Corrigan, Green, and Toomey, 1994; Morrison, Bellack, Wixted, and Mueser, 1990; Mueser et al., 1990), work skills (Anthony et al., 1995), overall social and occupational functioning (Breier et al., 1991). However, the relationships are modest explaining only a small portion of the variability. Also, many of these studies have an unintended confound in which negative symptom rating scales incorporate work and functional disability as signs used to rate avolition and apathy. Two examples are the Scale for the Assessment of Negative Symptoms (SANS)(Andreasen, 1981) and the Positive and Negative Syndrome Scale for

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Schizophrenia (PANSS) (Kay et al., 1987a). These rating scales also include items that relate to social functioning. For example, "inability to feel intimacy" and "relationships with friends and peers" are used to evaluate negative symptoms on the SANS as is the item "passive/apathetic social withdrawal" on the PANSS. Thus, what appears to be a correlation between functional disability and negative symptoms may actually be a replication of measurement within a single construct that is distinct from the construct of other symptoms of psychopathology. Hoffmann & Kupper (1997) reported factor analysis results that revealed the interrelation between measurements of psychopathology and social/vocational performance.

Another way in which studies unintentionally confound observed relationships between psychopathology and functional disability is that measures of global outcome generally incorporate symptomatology. For example, the Level of Functioning Scale, (Strauss & Carpenter, 1974) has items rating the presence of symptoms as well as items relating to hospitalizations. Therefore findings of relationships between symptoms and disability may be overestimates.

Neuropsychological Correlates of Functional Disability

Research has generally focused on the nature and extent of the NP impairment and not how these deficits impact the lives of the individuals. It is only very recently that the schizophrenia research literature has begun to address the possibility that NP impairment may be a determinant of functional disability. Meltzer et al. (1996) state in a recent article "Social and work function and overall outcome may be better predicted by persistent cognitive deficits than by residual psychopathology". Bilder (1997) in his review article on neuropsychological impairment in schizophrenia states that there is a

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growing consensus that NP deficits are pervasive and impact long-term outcome in a more direct and important way than psychotic symptoms.

Vocational Functioning

Meltzer et al. (1996) reported WCST performance was the best discriminator of employment status in 82 SZ subjects at baseline as well as in the remaining 76 patients at the 12 month followup. Measures of verbal fluency, verbal memory, attention and perceptuomotor speed were also found to discriminate between those employed and unemployed patients.

A preliminary study by this author (Berns, Jaeger, and Douglas, 1995) examined the predictive association between executive functioning (as measured by the WCST) and FD (assessed using the Social Adjustment Scale II; (Schooler, Hogarty, and Weissman, 1979)) in a diagnostically mixed group of outpatients (9 with SZ, 8 with schizoaffective disorder, 6 with affective disorders and 8 with personality and anxiety disorders). Multiple regression analysis revealed that WCST performance was significantly predictive of role functioning three months after discharge from a rehabilitation program independent of psychopathology, diagnosis and estimated IQ.

Lysaker et al. (1995) have shown that executive functioning, as measured by the Wisconsin Card Sorting Test, was significantly associated with work performance in 89 subjects with schizophrenia or schizoaffective disorder who were provided with jobs and assessed with the Work Personality Profile three weeks later.

These studies provide supportive evidence that NP dysfunction is related to vocational disability.

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Social Functioning

Several authors have argued that neuropsychological processes such as problem solving and reasoning are central to successful social functioning and that NP impairment may be a barrier in social skill training programs i.e. (Bellack et al., 1994; Liberman et al., 1986; Massel, Corrigan, Liberman, and Milan, 1991). Studies have consistently found a significant relationship between aspects of NP functioning and different aspects of social functioning. Performance on attention tasks has been found to relate to impairment in social skills (Penn, Mueser, Spaulding, Hope, and Reed, 1995), social cue perception (Corrigan et al., 1994) and social skill acquisition (Bowen et al., 1994; Kern, Green, and Satz, 1992). Verbal learning (Kern et al., 1992) and memory (Bellack et al., 1994; Corrigan et al., 1994; Mueser et al., 1991b) have been demonstrated to be significantly related to performance in social skills training and interpersonal problem solving. However, these studies have several limitations. All had small sample sizes (N=16-38), included inpatients only, and assessed few NP variables and circumscribed social behaviors.

Dickerson et al. (1996) studied the relationship between neuropsychological deficits, psychopathological symptoms and social functioning (as measured by the Social Functioning Scale (SFS)) in 88 stable outpatients with a diagnosis of schizophrenia or schizoaffective disorder. Canonical correlational analyses revealed significant relationships between social functioning (competence in activities of daily living, social activity and SFS total) and neuropsychological functioning (measures of language, visual motor, and spatial organizational abilities). There was also a significant relationship between social functioning as measured by the interpersonal communication scale of the

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SFS and the negative symptom and general symptom factors of the PANSS. There was no correlation between positive symptoms and social functioning. This study suggested that social functioning is best predicted by a combination of symptom and neuropsychological variables. Both the NP and PY variables were independently related to social functioning but taken together they accounted for 33% of the variance in total social functioning as measured by the SFS.

Residential Functioning

Wykes et al. (1990) found performance on a complex reaction time test predicted level of independent living in 28 chronic SZ patients followed for three years. This significant relationship remained in the second phase of this study, followup years four through six (1992). Performance on the reaction time test accounted for between 17 and 30% of the variance at all time points assessed.

Perlick et al. (1992c) found that a composite measure of neuropsychological functioning discriminated better than symptomatology, between a group of 26 chronically hospitalized patients and a group of 26 patients with a history of at least three years of community tenure without rehospitalization. A more recent study by Perlick et al. (1992b) used a comprehensive NP assessment battery. Memory, attention and motor summary measures discriminated inpatients from outpatients while language, conceptualization, and somatosensory summary measures did not.

Velligan et al. (1997) reports on two studies that examined the relationship between positive and negative symptomatology, NP functioning, and the ability to perform basic activities of daily living (ADL) in inpatients with schizophrenia or schizoaffective disorder. They hypothesized that positive symptoms, negative symptoms

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and NP deficits would all be related to ADL impairment but that symptomatology would not be related to ADL functioning after NP deficits were taken into account. They describe a model in which NP deficits contribute to symptomatology and ADL functioning. The first study (n=112) used The Brief Psychiatric Rating Scale to measure positive symptoms and the Negative Symptom Assessment to measure negative symptoms and global cognitive functioning (composed of items assessing orientation, abstracting ability, and short-term memory). The second study (n=41) used the same measures but used a more comprehensive neuropsychological assessment battery which included measures of attention, verbal and visual memory, fluency, and visual-spatial skills. Regression analyses revealed that NP function in both studies predicted over 40% of the variance in scores of ADL functioning. Symptomatology predicted a relatively small amount of variance in ADL.

Global Functioning

Several studies demonstrated significant relationships between NP impairment and overall outcome (combined functioning in several domains).

Goldberg et al. (1990) reported a strong correlation between neuropsychological impairment (including impaired performance on intelligence, executive, memory and attention measures) and ratings on the Global Assessment Scale (GAS) (Spitzer, Gibbon, and Endicott, 1975), a measure of overall social and vocational dysfunction, but not between NP performance and symptom ratings. Later studies by this group revealed that memory was a significant predictor of the difference in GAS scores between monozygotic twins discordant for SZ (1993) and that difference in GAS between monozygotic twins concordant for SZ was explained by difference in NP functioning

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(95% of the variance) and not by severity of their psychopathological symptoms or responsiveness to treatment (Goldberg et al., 1995).

Breier et al. (1991) also found a significant correlation between WCST impairment and overall outcome using the GAS.

Goldman et al. (1993) found that baseline memory dysfunction was associated with one year outcome (as measured by the total score on the Strauss-Carpenter Scale) in a sample of 19 inpatients with schizophrenia.

The International Pilot Study of Schizophrenia revealed that cross-sectional symptom manifestations are less important for explaining 11 year outcome than non-symptom variables such as previous interpersonal relationships, and extent of cognitive impairment (Carpenter & Strauss, 1991).

Goldman et al. (1998) examined the relative contribution of neuropsychological impairment and psychopathological symptom level to the prediction of functional outcome at two (N=64) and five years (N=32) after onset in a first episode sample. Multiple regression analyses used neuropsychological functioning (comprised of 6 composite scales: attention, language, memory, executive, motor and visual-spatial) and symptomatology (negative, positive and disorganized symptoms) as the predictor set and ratings on the Social Adjustment Scale as the outcome set. Symptoms did not relate to outcome at two or five years. The Attention Scale was significantly related to outcome at two years but not at five years (possibly attributable to the reduced sample size at five years).

Bilder's (1997) review of the literature concluded that NP performance before or early in the course of treatment (particularly on motor, attention and executive measures)

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accounted for 15-32% of the variance in long-term outcome while symptoms most often showed no significant relationship. He suggested that although the studies had methodological limitations and the predictive validity statistics may appear weak, NP impairment appears to be a relatively robust predictor of long-term functional disability.

Green (1996) reviewed 17 studies that assessed the relationship between neuropsychological impairment and functional outcome (including vocational and social functioning, social problem solving and psychosocial skill acquisition) in schizophrenic patients. This meta-analysis revealed that despite varied methodology, these studies consistently found a significant relationship between functional outcome and NP performance while not one of the reviewed studies found a significant correlation between positive symptoms and functional outcome. Negative symptoms were correlated with social problem solving and inconsistently with community functioning but the relationships were not strong especially in light of the overlap between the measurement of negative symptoms and functional disability as described previously. Also, different domains of NP functioning were found to relate to different aspects of functional outcome. Vigilance and immediate verbal memory (i.e., Digit Span performance) was associated with social problem solving and skill acquisition while performance on the WCST related to vocational functioning. Secondary verbal memory (i.e. recall of words after a delay) was found to correlate with all domains of functional outcome.

These findings are limited by the fact that each study in the review looked at only certain aspects of NP and FD. For example, the studies that looked at vocational functioning didn't study vigilance. Also, Green noted that the studies generally lacked sufficient power and were not hypothesis driven, using post hoc analysis. Given these

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problems, it is surprising that the findings were remarkably consistent across studies. Green recommended that future studies in this area need to move beyond general investigation (using only global measures of NP and FD) to evaluate whether specific NP domains are related to specific functional realms. Understanding the neuropsychological "rate limiting factors" would greatly improve cognitive remediation and rehabilitation efforts.

Liberman (1997) in a letter to the editor, commented on Green's review article described above. He pointed out several methodological considerations that may explain the lack of significant findings for psychiatric symptoms contributing to functional outcomes. He states that earlier studies used unreliable psychopathological assessments and often compared initial psychiatric symptoms with occupational outcome at a later time point. Restricted range in the symptoms may also be another factor to explain the low correlations between symptom severity and functional outcome. Liberman briefly describes an unpublished study where subjects were recruited from a wide variety of disorders, treatment programs and residential locations to ensure a range of symptomatology. He reported that cumulative severity of symptoms was the most important predictor of employability and employment. He goes on to recommend multidimensional studies to better understand the interactive relationships between psychopathology, psychiatric treatments, FD (including work, social support, reinforcement, disincentives) and NP functioning.

Two recent studies have used a multidimensional approach. Brekke et al., (1997), reported on the neuropsychological correlates of clinical and psychosocial functioning in 40 patients diagnosed with schizophrenia or schizoaffective disorder living in

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community-based settings. Performance on the WAIS-R Block Design subtest was significantly correlated with vocational disability while performance on the Digit Symbol subtest of the WAIS-R measures of executive functioning (verbal fluency and Stroop) were related to residential disability. There was no relationship found between NP measures and social functioning. Level of psychopathology, as measured by total BPRS ratings, was not significantly correlated with any of the measures of psychosocial functioning. A large multinational study employing Q-factor analysis with 495 subjects with mixed psychiatric diagnoses also demonstrated that the association between NP test performance and social and occupational history and background may follow a functionally specific pattern (Townes et al., 1985). For example patients with good verbal and memory functions and poor complex problem solving and motor functioning tended to be older, well educated unemployed females, while patients with poor verbal and memory functioning and good visual spatial problem solving and motor functioning tended to be younger, less educated males with histories of unskilled employment, learning disability and drug abuse.

Summary

Overall, findings suggest that NP impairment is significantly related to measures of functional disability. Furthermore, there is some evidence pointing to the possibility that specific domains of NP performance may be related to different aspects of functional disability. Studies examining the long-term course of SZ demonstrate that outcome is multidimensional and that there may be different determinants of different aspects of outcome (Carpenter & Strauss, 1991; Strauss & Carpenter, 1972; Strauss et al., 1974). Hogarty and Flesher (1992) stated "it is not at all clear how elementary or hierarchical

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(cognitive) deficits per se unilaterally or interactively relate to the specific instrumental and expressive role disabilities of schizophrenia. Before one embarks on the remediation of cognitive deficits, it would help to know how a specific deficit or pattern of deficits relates to schizophrenic disability." More refined analysis of the types of NP deficits most critical to disability may provide guidelines for more effective treatment strategies (including cognitive therapies, and pharmacologic intervention targeted toward improving NP impairment) as well as clues to the pathophysiology of schizophrenia.

CONCLUSIONS

The literature reviewed emphasizes several important points:

- Schizophrenia is heterogeneous with respect to symptom expression and course.
- Schizophrenia is the most functionally disabling of all psychiatric illnesses as well as the fifth most disabling medical disorder.
- Patients with schizophrenia have structural and functional brain abnormalities, however the pathophysiology of schizophrenia is unclear.
- Patients with schizophrenia have neuropsychological impairment in attention, memory, motor, executive and language functions.
- NP deficits are not secondary to other aspects of the illness such as psychopathology, institutionalization and neuroleptic treatment.
- Psychopathological symptomatology is a modest determinant of functional disability.
- NP impairment has been significantly associated with global functioning as well as disability in vocational, social and residential domains.

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THE PRESENT STUDY

The present study aimed to improve upon the methodological limitations of previous studies. Many used only global measures of functioning, used inadequate neuropsychological assessments and had small patient samples that were generally selected from a hospitalized cohort or program which restricted the range of levels of functional disability. Few studies have looked at the inter-relationships between NP functioning, symptomatology and FD. The present study sampled 60 patients with schizophrenia enrolled in an outpatient clinic. This allows for a wide range of functional disability. A battery of NP assessments was used to assess functioning in five domains: attention, memory, executive, language and motor. FD was also assessed multidimensionally with measures of social functioning as well as a new measure of FD that separately rates the role position held by the subject, the amount of support utilized, and performance level in the vocational, educational and residential domains. Psychopathological symptom ratings were assessed concurrently.

The primary hypothesis was that NP performance would correlate with FD independent of psychopathology. Furthermore, NP performance and psychopathology would relate to different aspects of functional disability. Understanding the independent contributions of NP impairment and psychopathology to FD would provide a guide for the development of more effective interventions for the chronic functional disabilities of schizophrenia.

METHODS

This study utilized a multidimensional cross-sectional design to determine inter-relationships among five domains of NP functioning (memory, attention, executive, motor

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and language), symptoms of psychopathology, and types of functional disability (including vocational, social, and residential) in a sample of outpatients with schizophrenia.

SUBJECTS

Subjects were 60 consenting patients randomly selected from those registered in the ambulatory clinic at Hillside Hospital with a diagnosis of schizophrenia who met the inclusion criteria of: (1) age between 18 and 45 (to focus on patients during the period of their lives when they are most impacted by the vocational disability); (2) history of a psychotic disorder for at least 5 years; (3) confirmation of schizophrenia diagnosis using the Structured Clinical Interview for the DSM IV (SCID); (4) fluency in English; (5) no history of a primary neurological disorder; (6) no active substance abuse defined as evidence of alcohol or drug use that caused persistent or recurrent functional disability in the past six months (7) time since psychiatric hospitalization of more than three months (to allow for stabilization of symptoms and functioning) and (8) no diagnosis of mental retardation.

Hillside Hospital is part of Long Island Jewish Medical Center. It is a 225 bed tertiary care psychiatric specialty hospital that serves a culturally and socioeconomically diverse constituency. The ambulatory clinic provides outpatient psychiatric care including the services of a psychiatrist as well as individual and group psychological therapy. For most of the patients in the present cohort, the ambulatory clinic is providing aftercare following an inpatient hospitalization at Hillside Hospital. Sampling from an ambulatory clinic is optimal for the present study as it provides for the maximum range of functioning from among ambulatory patients with schizophrenia. This is a very heterogeneous group including patients that are engaged in no productive activity to those

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that work full-time. This excludes patients in need of comprehensive care services such as inpatient hospitalization, partial hospitalization and continuing day treatment. While perhaps the ideal study would utilize an epidemiological sample representing all people with SZ, this is practically extremely difficult and has never been fully accomplished. The most critical problem is our lack of understanding of the determinants of functional disability in the community (Velligan et al., 1997). What makes it difficult for people with SZ to get a job, live on their own, go to school, have friends and get married? These are crucial questions not fully addressed in the literature. Almost all of the studies to date have looked at correlates of functional disability in inpatients. This study aimed to sample the widest range possible of outpatients with schizophrenia.

The sampling method involved obtaining lists of all clinic registrants, randomly selecting 60 of these cases who met criteria, and approaching these patients to obtain informed consent. As patients were encountered who refused to participate, the process was repeated until 60 patients consented to the study. The total number of possible subjects in the pool from which the 60 were drawn was 269. Forty-three patients (who appeared to meet criteria for inclusion in the study based on chart review only) refused to participate.

In order to determine whether the sample obtained was a good reflection of the population from which it was drawn, consenting patients were compared to the pool of 269 possible participants with respect to gender, diagnostic subtype, and age. A significant difference in the diagnostic subtype distribution was found between the groups such that the consenting subjects had a larger percentage of paranoid subtype diagnoses (see Table 1).

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Table 1: Comparison between Consenting Subjects and Possible Subjects

	Possible Subjects			Consenters			Statistic (F or Chi Square)	
Variables	**n**	**Mean**	**SD**	**n**	**Mean**	**SD**	**df**	**p**
Age	269	35.08	6.55	60	35.85	5.50	99	.35
	n	**%**		**n**	**%**		**df**	**p**
Gender							1	.11
Male	173			45	75			
Female	96			15	15			
Diagnosis Subtype							1	.15[1]
Paranoid	176	65		45	75			
Undifferentiated	53	20		13	22			
Disorganized	8	3		1	1.7			
Catatonic	2	.7		0	0			
Residual	6	2.3		1	1.7			
Not specified	23	9		0	0			

[1] This analysis is based on a merging of the categories into paranoid and non-paranoid diagnostic groups.

Consenting patients were also compared with refusing patients with respect to age, race, gender, education, diagnostic subtype from chart diagnosis, age of onset of psychiatric treatment, and recency of last hospitalization. The analyses performed were t-tests for the continuous variables and chi-square tests for the categorical variables (see Table 2). Due to small cell sizes, education was collapsed into three categories (GED/no diploma, high school diploma, and above a high school diploma), SZ subtype was collapsed into paranoid and non-paranoid types, and race was collapsed into two categories (Caucasian and non-Caucasian) for the analysis.

Group comparisons yielded no significant differences between those who entered the study and those who refused on race, education, time since discharge from last hospitalization, diagnostic subtype, or age at onset of symptoms. The two groups were significantly different with respect to age first treated by a mental health professional ($t=2.1$, $p=.04$) such that the consenters were younger at the time of first treatment than the refusers (mean (SD)=21.2 (5.4) and 23.5 (5.2) years of age respectively). This suggests

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that the refusing group might be less sick and possibly less impaired. This variable is based on the subject's recall as well as chart records, however, the accuracy of such data is questionable. A non-significant trend was observed with respect to gender such that men accounted for 75% of the consenting sample but only 58.1% of the refusing sample (Chi-Square=3.27, p=.09). This gender difference may be due to several factors. Although the prevalence of schizophrenia is roughly equal in men and women, men are more disabled and may utilize more services. Also, there may be a gender bias in this sample towards women refusing to participate in the project. This may also explain the later onset of treatment finding as women with SZ tend to have a later onset than men.

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Table 2: Comparison between Refusing and Consenting Subjects

	Refusers			Consenters			Statistic (F or Chi Squared)	
Variables	**n**	**Mean**	**SD**	**n**	**Mean**	**SD**	**df**	**p**
Age	43	36.25	5.82	60	35.85	5.50	99	.73
Years of Education	43	13.17	1.69	60	13.45	1.67	101	.41
Age first treated by mental health profess.	41	23.46	5.21	60	21.22	5.39	99	.04 *
Time since last hosp (yrs)	42	4.99	3.92	60	5.18	4.01	100	.81
Variables	**n**	**%**		**n**	**%**		**df**	**p**
Race							1	.98[1]
Caucasian	30	70		42	70			
African American	10	23		14	23			
Hispanic	2	5		1	2			
Asian	0	0		3	5			
Native American	1	2		0	0			
Highest Degree							2	.52[2]
None	2	5		1	2			
High School	31	72		39	65			
GED	5	11		9	15			
Associates	2	5		4	6			
BA	2	5		6	10			
MA	1	2		1	2			
Gender							1	.088**
Male	25	58		45	75			
Female	18	42		15	15			
Diagnosis Subtype							1	.56[3]
Paranoid	30	70		45	75			
Undifferentiated	11	26		13	22			
Disorganized	0	0		1	2			
Catatonic	1	2		0	0			
Residual	1	2		1	2			

[1] This analysis is based on a merging of the categories into Caucasian and non-Caucasian groups.
[2] This analysis is based on a merging of the categories into GED/no degree, high school degree, and above a high school diploma groups
[3] This analysis is based on a merging of the categories into paranoid and non-paranoid diagnostic groups.
*statistical significance < .05
**statistical significance <.1

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Participants included 45 men and 15 women with the mean age of 35.9 (SD=5.5) which ranged from 22.6 to 44.9. The ethnic distribution of the sample was the following: 42 Caucasian, 14 African-American, 1 Hispanic, and 3 Asian.

The age of onset of symptoms (based on self-report and chart review) ranged from 5 to 38 years with an average age of 20.4 years (SD=5.9). The average age of initial psychiatric treatment was 21.2 years (SD=5.4) and ranged from 10 to 38 years.

Education averaged 13.5 years (SD=1.8) with one completing the tenth grade, 48 completing high school or the equivalent, and 11 attending or completing college. Of those who went to college, they completed an average of 55.0 credits (Range=3-200, SD=55.8). Most of these participants went to several colleges over many years with four completing an Associates degree, six a Bachelors degree, and one a Masters degree. Twenty-two subjects attended a certificate or trade school an average of 3.7 months (Range=1-32, SD=7.5). Half of these subjects attended these programs part-time and half attended full-time. Eight subjects reported illness related interruptions in their education that required them to miss a significant amount of time in school or caused them to drop out during or prior to high school and 27 reported interruptions after high school. Thirteen subjects reported being held back to repeat a grade in school and 6 attended special education classes.

Of the 60 subjects, 25 were working for pay at the time of participation and 35 had not worked for pay for five years prior to participation. Of those currently working, 10 had held that job for less than one year, 11 between one and four years, and 4 more than four years. Five were working less than 12 hours per week, 9 between 13 and 30 hours, and 11 were working full time. Twelve of these jobs were at or below minimum

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wage and 13 were above minimum wage. Six subjects utilized some supportive service for getting and/or maintaining the job including an off-site job coach, in-house transitional work and work crew programs. Using the Hollingshead coding scheme for categorizing employment (Hollingshead, 1975) where a rating of one is given for jobs requiring only manual labor and a rating of nine is given for major professionals and executives, ratings for jobs held currently by the subjects averaged 4.0 (SD=1.8). Eight were in the 1 to 3 range (unskilled-semiskilled work), 12 were in the 4 to 5 range (skilled manual work/clerical work), and 5 were 6-7 (technicians and minor professionals).

Of the remaining 35 not engaged in paid employment: 1 was a caregiver for an elderly family member, 5 worked at a volunteer job (1 full-time, 4 part-time), 2 attended part-time college, 4 participated in a non-mainstream vocational training program (1 full-time, 3 part-time), 6 attended a psychiatric rehabilitation program (4 full-time and 2 part-time), and 17 (28.3%) were idle.

A plurality of the sample lived at home with their parents (30) while 12 lived in supported housing and 18 lived on their own or with a friend or spouse. The marital status of the sample was as follows: 48 never married, 5 married, 6 divorced and 1 separated. All subjects were fluent in English (53 spoke English as first language and the remaining 7 learned English before age 10). The diagnostic distribution of subtypes of schizophrenia were 45 paranoid, 11 chronic undifferentiated, 3 residual, and 1 disorganized. All 60 patients were taking neuroleptic medication. Using a dose equivalency model (Schooler, 1993), 19 received a low dose, 23 a moderate dose, 13 a moderately high dose, and 5 a high dose of antipsychotic medication. The overall

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intelligence of the sample fell into the average range (VIQ=94.7 (SD=12.1, Range=72-130), PIQ=91.1 (SD=13.53, Range 67-130), FSIQ=92.4 (SD=12.1, Range=70-134)).

PROCEDURE

If the patient consented to participate (see consent form in Appendix 1), the Structured Clinical Interview for the DSM IV (SCID) Mood and Psychotic modules (First, Spitzer, Gibbon, and Williams, 1995) were administered to ensure the diagnosis of schizophrenia and the subject was screened for the remaining inclusion criteria (described above in the subjects section page 42).

If the subject met the inclusion criteria, the functional disability measures and symptom ratings (described below) were administered in approximately two hours. The neuropsychological assessment (described below) was then administered in approximately three hours. The assessments were administered at each participants own pace with breaks and continuation on another day as necessary with most taking two days for completion.

Patient confidentiality was assured through code number assignments in place of names, controlled access to data with computer coding, and a secured file room.

MEASURES

All measures were administered by this author or one of two staff members at the Hillside Hospital's Center for Neuropsychiatric Outcome and Rehabilitation Research (CENORR) where this author is supervisor. These two staff members were rigorously trained and supervised by this author following established training protocols and testing procedures. Interrater reliability coefficients for the functional disability and

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psychopathology measures ranged from .86 to .94. All assessment data were checked for accuracy by this author. See Table 3 for a list of all assessments administered.

Table 3: Summary of Measures

Diagnostic Interview	Neuropsychological Assessment
Structured Clinical Interview for the DSM-IV (SCID)	Wisconsin Card Sort Test (WCST)
	Ruff Figural Fluency (RUFF)
Psychopathology	Letter Number Span (LNS)
Brief Psychiatric Rating Scale (BPRS)	Concentration Endurance Test (d2)
	Wechsler Memory Scale-Revised (WMS-R)
Functional Disability	Wechsler Adult Intelligence Scale-Revised (WAIS-R)
Social Adjustment Scale-II (SASII)	Grooved Pegboard Test (GP)
Multidimensional Scale of Instrumental Functioning (MSIF)	Finger Tapping Test (FTT)
Global Assessment of Functioning Scale (GAF)	Controlled Oral Word Association Test (COWAT)
Social and Occupational Functioning Assessment Scale (SOFAS)	Animal Naming Test (ANT)
Hillside Neurorehabilitation History Form	Boston Naming Test (BNT)

Diagnostic Interview

The Structured Clinical Interview for the DSM-IV (SCID) (First et al., 1995) Mood and Psychotic modules were used to confirm the chart diagnosis of schizophrenia. This is the current standard for assuring accurate diagnosis using the DSM-IV criteria which allows for comparison across studies (Ventura, Liberman, Green, Shaner, and Mintz, 1998)..

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Psychopathology Ratings

For the purpose of this study, psychopathology is used as a term for the psychotic symptoms most characteristic of SZ and does not include other characteristics that could also be termed psychopathology such as personality traits.

The Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1988) is the most widely used measure of psychopathology in the schizophrenia literature (Hafkenscheid, 1991). Eighteen signs and symptoms are rated on a scale from one to seven (1=not present, 2=very mild, 3=mild, 4=moderate, 5=moderately severe, 6=severe, 7=extremely severe). BPRS factor scores derived by Guy (1976) were used in the analyses. These factors are computed as follows: a) the Anxiety Depression Factor is comprised of somatic concern, anxiety, guilt and depressive mood; b) the Anergia Factor is comprised of emotional withdrawal, blunted affect, motor retardation, and disorientation; c) the Thought Disturbance Factor is comprised of conceptual disorganization, grandiosity, hallucinations and unusual thought content; d) the Activation Factor is comprised of tension, excitement and mannerisms and posturing; and e) the Hostility Factor is comprised of hostility, uncooperativeness and suspiciousness. Factor scores are computed by summing the ratings on the factor items and dividing by the number of items. Thus, the factors have the same 7 point scale. A review of psychometric studies of the BPRS found it to be a sensitive and effective measure of psychopathology (Hedlund & Vieweg, 1990). It has been used in the majority of psychopharmacologic trials (ie. (Volavka, Cooper, Czobor, and Meisner, 1995)) as it reliably measures treatment response. It is considered the gold standard by which other rating scales are validated (ie. Bell, Milstein, Beam, Lysaker, and Cicchetti, 1992; Morlan & Tan, 1998). Its construct

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validity has been established in several ways including a factor analysis (Guy, 1976; Overall, Hollister, and Pichot, 1967) and redundancy analysis (Czobor, Bitter, and Volavka, 1991). Anchors (Woerner, Mannuzza, and Kane, 1988) and training tapes are available which readily permit the achievement of high inter-rater reliability. Bell et al. (1992) report an inter-rater reliability of .87 for the total scale.

Functional Disability Measures

The Social Adjustment Scale II (SASII) (Schooler et al., 1979) was chosen as it represents a standard in the field for global ratings of FD in vocational and social domains. It is an adaptation of the Social Adjustment Scale (Weissman, 1975) specifically designed for use with ambulatory individuals with chronic schizophrenia (Wallace, 1986). It is a semistructured interview of 52 items that include measurement of role functioning (work, school, homemaker), relationships with household members, relatives and friends, leisure activities and personal well-being. This measure has been used in many large scale, multicenter studies evaluating the efficacy of neuroleptics and longitudinal outcome studies of schizophrenia (ie. Schooler, Keith, Severe, and Matthews, 1989). The SASII is considered a standard to which other measures of functioning are compared (ie. Good Ellis, Fine, Spencer, and DiVittis, 1987; Munroe-Blum, Collins, Nuttall, and McCleary, 1993). A reliability study of 56 SZ patients and their significant others revealed excellent agreement between the two groups (Spearman's rank correlation coefficient rho =.98) (Weissman, Sholomskas, and John, 1981). The global ratings for Social Leisure, Instrumental Role Performance and General Adjustment were used in the analyses. Information was collected from at least two sources to ensure

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validity of the data: the patient, and at least one corroborating source such as medical chart, family member, friend, or health professional (with patient's prior consent).

The Multidimensional Scale of Instrumental Functioning (MSIF), developed by Jaeger and Berns (1997), was also used as it incorporates features not addressed in the other FD measures. Essential to research in this area is the measurement of functional competencies in a manner that permits comparison of data across a wide range of geographically and socioeconomically heterogeneous research environments (Attkisson et al., 1992). Both Weissman (1975) and Wallace (1986) note that none of the instruments they reviewed is wholly adequate for assessing functioning and cite a strong need for standardization of methods between studies. Anthony & Liberman (1986) indicate the importance of the assessment of an individual's competencies as well as the identification of the environmental demands and support available to the individual. Some measures globally assess the assistance received from others (e.g. the MRSS, Affleck & McGuire, 1984, and RFS, Goodman, Sewell, Cooley, and Leavitt, 1993) with level of support treated as a measure of the patient's functioning which assumes that the availability of support is uniform for all patients. Since support systems vary across service systems, ratings from such instruments cannot be compared across research sites. Several authors have stated the need for assessing functioning multidimensionally (Green & Gracely, 1987; McGlashan, Carpenter, and Bartko, 1988). The MSIF attempts to incorporate these recommendations by independently rating the dimensions of Role Position, Support and Performance (given the role position and level of support), in each of three environments: Work, Education (if applicable for a given patient) and Residential. Role Position refers to the actual role the individual is expected to perform.

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Support refers to the amount of assistance an individual receives in the specified role position. Performance refers to the quality of the productive activities within the role environment as well as their timeliness and the reliability with which they are performed. Based on these nine ratings, global ratings are made across domains (Global Role Position, Global Supports, and Global Performance) and within environments (Global Work Functioning, Global Educational Functioning-if applicable) and Global Residential Functioning). Finally, an overall independent functioning global or "Global, Global" rating is made indicating the level of functioning (or conversely level of disability) across all domains and within all environments. Explicit anchors and guidelines are provided for each of these ratings. Table 4 illustrates the 16 ratings thus obtained with the MSIF. The Global Role Position (representing the role responsibility combined across the three domains of work, education and residential), and Global Independent Functioning ratings (which takes into account the role position as well as the support and performance levels) were used in the statistical analyses.

Table 4: Schematic Representation of the MSIF

	Role Position	Support	Performance	Global
Work				
Education				
Residential				
Global				

The psychometric properties of this scale were examined in 114 consenting patients enrolled in Hillside Hospital's psychiatric clinic or in one of its affiliated rehabilitation programs. Each patient was administered a brief demographic interview, the Social Adjustment Scale II (SASII) and the MSIF. The sample was comprised of 65% men, 70% Caucasian, 22% African-American, 3% Hispanic and 5% Asian. The age

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ranged from 18-50 with a mean age of 34.2 years (SD=7.51). Diagnoses were 87% schizophrenia spectrum, 9% affective disorder, and 4% ADHD or OCD. Four percent of the sample had less than a high school education while 37% completed high school or the equivalent, 34% completed some college, and 15% completed at least a 4-year college degree.

Criterion validation of the MSIF was tested against the Social Adjustment Scale II (SASII) yielding a highly significant correlation between these two scales. Table 5 presents Pearson Correlation Coefficients for comparable global ratings:

Table 5: Correlation of Global Indices

	SASII Instr. Role Perf.		SASII Gen. Adjustment	
	R	**p**	**R**	**P**
MSIF Global Role Position	.84	.001	.78	.001
MSIF Global FD	.85	001	.80	.001

The Global Assessment of Functioning (GAF) Scale and the Social and Occupational Functioning Assessment Scale (SOFAS) from the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) (American Psychiatric Association, 1994) were also used. The GAF rates the subject's overall psychological, social and occupational functioning. The SOFAS focuses exclusively on impairment in social and occupational functioning and is not directly influenced by severity of psychological symptoms.

The Hillside Neurorehabilitation History Form was used to obtain the following information: demographic information (e.g. age, race), age of onset of psychotic symptoms and treatment, hospitalization and other mental health service utilization, current medication and their side effects, as well as education and work history .

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Information was collected from at least two sources to ensure validity of the data: the patient and at least one corroborating source such as a medical chart, family member, friend, health professional (with patient's prior consent).

Neuropsychological Measures

This neuropsychological test battery was assembled on the basis of a comprehensive review of neuropsychological tests tapping each of the principal domains of functioning that have been shown to be impaired in patients with schizophrenia (e.g. Lezak, 1995; Spreen & Strauss, 1998). The domains of functioning and the tests comprising each domain are described below. While no neuropsychological measure is a pure assessment of a domain, the tests are listed under the domain to which they contribute the most. Each domain is represented by a minimum of two measures. Redundancy of measurement within each domain is essential to the valid interpretation of test results in neuropsychology and represents a standard of practice (Lezak, 1995). The assessments were administered in one of two orders (order 1 is seen in Table 3, pg. 50, the second order is the reverse). These orders were derived using two main criteria. First, one test in each domain was given in the first half of the battery to be able to have some data in case the subject refuses to continue. Also, the "harder" tests were followed by "easier" tests to try to keep the subject motivated to complete the battery.

Memory

The Wechsler Memory Scale - Revised Edition (WMS-R) (Wechsler, 1987) is a standard battery for the measurement of memory and learning (Lezak, 1995). Extensive administration and scoring instructions are provided in the manual. The norms for this test are based on 300 cases designed to represent the normal population of the United

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States between the ages of 16 and 75 (Spreen & Strauss, 1998). The subtests used in the analyses for the present study included Logical Memory I and II (the immediate and delayed recall of short stories) as well as Visual Reproduction I and II (the immediate and delayed recall of line drawings). Test retest reliability coefficients for these subtests range from .71 to .87 (Spreen & Strauss, 1998). Strong correlations are consistently found between these subtests and other memory tests (Lezak, 1995). Extensive validity studies are described in the manual. Factor analysis revealed similar patterns with normals and mixed clinical samples (346 patients with memory impairment) as well as with a younger and older age groups. The clinical group scored significantly lower than the normal group on all WMS-R Index Scores (composites of the subtests) with effect sizes in the moderate to large range (.71-1.11). Also, a group of 14 chronic SZ patients performed significantly worse than the normal group on all Index Scores (Wechsler, 1987). This scale was chosen over using several individual memory tests since it has redundancy already built into it and uses a very large normative database.

Executive Functioning

The Wisconsin Card Sorting Test (WCST) is a widely used measure of executive functioning (Grant & Berg, 1995). This test has received considerable attention since the demonstration by Goldberg et al. (1987a) that schizophrenic patients may have persistent deficits on the task even after explicit instruction. It focuses on the subject's ability to generate hypotheses, establish response sets, and switch sets by sorting stimulus cards on the basis of one of 3 perceptual attributes (color, form, and number). The only feedback provided by the administrator is whether each response is correct or incorrect. The sorting rule is changed after 10 consecutive correct responses. Testing is completed

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when the subject has completed 6 correct categories or reached the maximum number of 128 trials. Standardized scoring procedures are available (Heaton, 1981a). Normative data are based on a sample of 384 normal controls. A preliminary study suggested that number of perseverative errors on this test was predictive of role functioning impairment (Berns et al., 1995). Number of categories completed and perseverative errors were used in the statistical analyses.

The Ruff Figural Fluency Test (RFFT) (Ruff, Light, and Evans, 1987) assesses divergent thinking, the ability to shift cognitive set flexibly and the ability to use planning strategies (Spreen & Strauss, 1998). The RFFT has five parts each containing 35 identical stimuli arranged on 8.5 x 11 inch sheets of white paper that vary in the pattern of the dots and by the use of distracters. Subjects are asked to draw as many different designs as possible in 60 seconds by connecting at least two dots or more than two dots with a straight line. Number of unique designs and perseverative errors were used in the statistical analyses. The manual provides normative data for 358 subjects broken down by age and education as well as extensive instructions for standardized administration and scoring. Test-retest reliability was determined by repeating the test with a representative subset (N=95) of the normative sample after six months (Ruff et al., 1987) yielding a correlation coefficient of .76 for unique designs and .36 for perseverations. Construct validity studies have found similar factorial structures in normals and head injured patients supporting its measurement of initiation, planning, and divergent reasoning (Baser & Ruff, 1987). Interrater reliabilities for number of unique designs and perseverative errors of .93 and .74 respectively have been reported (Berning, Weed, and Aloia, 1998).

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Attention/Working Memory

The Concentration Endurance Test (d2 test) is a type of cancellation test developed by Brickenkamp (1981) where the subject is asked to visually scan, locate, and "cancel" (by marking with pencil) target stimuli that are embedded in an array of distracting stimuli. The test has 14 lines with 47 letters in each line. There is a 20-second per line time limit. Cancellation tests have been used widely in clinical and experimental neuropsychology as measures of vigilance. Normative data given in the test manual are derived from large samples (n=3,132) of normal students and adults ages 9 to 60 years. Internal consistency is found to be approximately .8 and test-retest reliability is high, approximately .9 after a 5 hour interval and .92 after a 12 month interval. The d2 test has show strong correlations with other tests of attention including the Digit Symbol subtest of the WAIS-R and factor analyses consistently report high loadings on attention (Spreen & Strauss, 1998). The total number of errors was used in the analyses.

The Letter Number Span Test (LNS) developed by Gold et al. (1997) is purportedly a measure of auditory working memory. The administrator lists numbers and letters and the subject must repeat the numbers first in ascending order and then the letters in ascending order. For instance if the administrator says, " 5t9a", the correct answer would be "59at". There are 24 items in all and the string lengths' range from 2 items to 7 items. There are 4 trials of each string length. If the subject fails all trials in a single row the test is discontinued. The score used is the total number correct. This test is found to have a high degree of internal consistency (Cronbach coefficient $\alpha = .85$). Normative data are reported on a sample of 30 normal controls. An adapted version of this test is part of the newly revised Wechsler Adult Intelligence Scale-III. Gold et al.

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(1997), administered both the LNS and the WCST to 30 normal controls and 36 patients with schizophrenia. LNS performance was highly correlated with WCST performance (r=.74) and between group differences in performance on the WCST were eliminated when LNS score was covaried. This finding suggests that impaired performance on the WCST may in fact reflect a working memory deficit.

The Visual Span Backwards and Digit Span Backwards subtests of the WMS-R (described above) were also used in the statistical analyses.

Motor

A modified version of the Edinburgh Handedness Inventory described by Oldfield (1971) was used to determine hand preference. In this version, subjects are asked to perform a variety of actions with imagined objects. The scores for right and left-hand responses are totaled separately and are converted to a laterality quotient. This will determine the dominant hand for the Finger Tapping Test and Grooved Pegboard Test.

The Finger Tapping Test (FTT) is a widely used motor speed test that is administered using a mechanical finger tapper and has received extensive clinical and research use as part of the Halstead-Reitan Battery (Reitan & Davidson, 1974). Administration includes a minimum of 5 10- second trials with each hand, and total number of taps on each trial are recorded. Administration continues until there are 3 trials within 5 "taps." The score for each hand is the mean of the highest 3 trials within 5 taps. Normative data are provided for 365 normal controls grouped by age, sex and education (Bornstein, 1985). The score for the non-dominant hand was used in the analyses due to a missing case for the dominant hand. The high correlation between the

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dominant and non-dominant hand scores for this sample (r=.81, p=.00) supports this choice.

The Grooved Pegboard Test (GPT) is a component of the Wisconsin Neuropsychological Test Battery (Matthews & Love, 1964). This was chosen over the Purdue Pegboard Test since it is a more sensitive measure of fine motor skills that is extensively used in vocational testing. It requires that the subject place ridged pegs into a 5 x 5 grid of angled slotted holes. The peg has to be rotated into the proper orientation for insertion. The task is timed and assesses manipulative agility and complex coordination using both the preferred and non-preferred hand. Bornstein et al. (1985) has also provided normative data on this test with the same sample of 365 controls. The score used is the time to complete insertion of all 25 pegs. The score for the dominant hand was used in the analyses.

Language

These language tests are sensitive to difficulties in productive speech that individuals with schizophrenia have such as perseverations (incorrectly repeating the same word), intrusions (saying a word that doesn't fit the "rule") and slowing (Barr, Bilder, Goldberg, Kaplan, and Mukherjee, 1989).

The Controlled Oral Word Association Test (COWAT) is part of the Multilingual Aphasia Examination (Benton & Hamsher, 1978) that measures phonemic verbal fluency. It requires the subject to produce as many words as possible that begin with specific letters in a 60 second period, with the restrictions that there be no repetitions, no different forms of the same word, and no proper nouns. Two sets of letters (CFL and PRW) are used as alternate forms of the test and are matched according to the frequency of English

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words beginning with these letters. The score is the sum of all correct words produced during the three trials. Normative data are based on a sample of 360 normal subjects with ages ranging from 25-64 years with equal cell size for sex and education. No age effects were seen and gender differences were seen to be insignificant. Retest reliability after 19-42 days has been reported as .88 (Spreen & Strauss, 1998).

The Animal Naming Test, a subtest from the Boston Diagnostic Aphasia Examination (Goodglass & Kaplan, 1983) measures semantic verbal fluency. It requires the subject to name as many animals as possible for a 90-second period. The final score is the number of animals named during the most productive 60 seconds. Norms are provided in Spreen and Strauss (1998) and are based on community volunteers in Ottawa, Ontario stratified by age and education with 187 people between the ages of 16 and 59.

The Boston Naming Test is a test of visual confrontation naming from the Boston Diagnostic Aphasia Examination (Goodglass & Kaplan, 1983). The subject is asked to name objects depicted in 60 line drawings that increase in difficulty. If the subject is unable to name an item correctly after 20 seconds, the examiner provides a contextual and/or phonemic cue. The scoring is based on the sum of the number of correctly named items and the correct responses to contextual cues. Normative data were provided on 84 adults and were classified by age.

Intelligence

The Wechsler Adult Intelligence Scale - Revised (WAIS-R) (Wechsler, 1981) is the most extensively used and best standardized measure of intellectual functions. IQ and individual subtest score patterns have been validated in discriminating healthy controls from neurological and psychiatric samples (Lezak, 1983; McFie, 1975). The WAIS-R

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comprises 6 verbal subtests and 5 performance subtests, which test language, attention, executive and visuospatial functions. These tests render separate subtest raw, scaled and age corrected scaled scores, and the composite Verbal, Performance, and Full Scale intelligence quotients. The IQ scores were used for descriptive purposes and the vocabulary subtest was used as a covariate in the statistical analyses. Explicit administration and scoring procedures as well as information on reliability and validity are furnished in the manual. Normative data was obtained on 1,880 people. Split half coefficients are very high (.97, .93, .97, .96 for Verbal IQ, Performance IQ, Full Scale IQ, and vocabulary respectively). The vocabulary subtest is correlated with the Full Scale IQ at .81 and at .85 with the Verbal IQ. Test-retest reliability coefficients are presented for readministration (N=71, ages 25-34) within two to seven weeks (.94,.89, .95,.93 for Verbal IQ, Performance IQ, Full Scale IQ, and vocabulary respectively). Validity has been established through correlation with other intelligence tests such as the Stanford Binet (r=.85), through factor analysis, and correlations with academic success (r=.50).

RESULTS

Overall findings support the hypothesis that NP impairment and psychopathology are separate contributors to FD. Descriptive analyses of the NP assessment, psychopathology ratings and FD measures are presented. The results of the primary analysis, a canonical correlation examining the relationship between neuropsychological deficits and measures of functional disability controlling for the contribution of psychopathology and verbal intelligence is described. Finally, secondary analyses further exploring the inter-relationships between NP deficits, psychopathological symptoms, and types of functional disability are presented.

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NEUROPSYCHOLOGICAL FUNCTIONING

Performance of the participants on the neuropsychological measures used in the analyses is summarized in Table 6. The z-scores reflect the participants' performance relative to the normative data provided with each test or taken from the literature (as specified in the methods section above). The results indicate below average performance for these participants across all domains with no notable patterns of selective deficit or preservation. Mean Z scores for tests within the language domain range from .02 to -1.59, .17 to –2.61 within the motor domain, -.34 to –1.01 within the executive domain, -.32 to –1.22 within the attention domain, and -.25 to –1.01 within the memory domain. Aggregate data precludes the analysis of patterns of deficits at the individual level. Since z-scores were calculated based upon disparate normative samples, comparisons of mean z-scores to estimate level of relative deficit between different tests would most likely be unreliable. The range of scores seems adequate and the interquartile values (reflecting the spread of the data for the middle 75% of the cases) indicate that the distribution is not significantly skewed. The analysis of the effect of the order in which the neuropsychological assessments were administered was not significant.

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Table 6: Neuropsychological Performance of Participants-Raw Scores and Z Scores (N=60)

		RAW SCORES				Z SCORES			
Domain	**Variable**	**Mean**	**SD**	**Range**	**Inter-quartile**	**Mean**	**SD**	**Range**	**Inter-quartile**
Language	BNT Total Correct	51.23	6.32	35-60	8.50	-1.59	2.19	-7.62,1.62	2.66
	COWAT Total Correct	39.37	10.34	16-60	14.00	.02	1.09	-2.39, 2.07	1.52
	ANT Total Correct	17.58	5.13	7-30	5.75	-.69	1.07	-2.76,1.71	.86
	WAIS-R Vocabulary	43.47	12.32	16-65	19.75	-.31	.89	-2.67,1.67	4.00
Motor	GP Non-Dominant Time	118.22	79.04	54.3-600	48.38	-2.61	3.03	-15.80,1.27	2.79
	FTT Dominant Time	44.88	9.56	23-60.66	14.83	-.08	1.5	-3.72,2.58	2.12
	D2 Total Letters	401.88	72.95	200-552	107.50	.17	.66	-1.73,1.53	14.00
	WAIS-R Digit Symbol	47.47	11.91	20-77	15.50	-.62	.83	-3,1.67	2.75
Executive	WCST Perseverative Errors	24.13	19.61	4-94	25.75	-.9	1.57	-6.51, .72	2.07
	WCST Categories	3.92	2.17	0-6	4.00	-.83	1.42	-3.41, .54	2.63
	RFFT Perseverative Errors	12.15	15.83	0-81	11.75	-.34	1.58	-6.04,1.11	1.37
	RFFT Unique Designs	71.63	22.90	20-141	26.25	-1.01	1.19	-3.7,2.11	1.36
Attention	LNS Total Correct	12.52	3.96	3-21	5.00	-1.22	1.5	-4.88,2.04	1.92
	WMS-R Visual Span Backward	7.08	2.00	2-11	2.75	-.35	1.01	-3.53,1.62	1.33
	WMS-R Digits Backward	6.12	2.08	3-12	2.00	-.32	1.01	-2.41,2.48	.96
	D2 Errors	21.8	31.43	1-202	21.00	-.03	1.37	-7.87, .87	.91
Memory	WMS-R Logical Memory I	17.87	6.85	4-31	8.75	-1.01	.89	-2.75,.63	1.27
	WMS-R Visual Repro. I	31.3	6.97	15-41	10.00	-.25	1.31	-3.30,1.60	2.03
	WMS-R Logical Memory II	12.85	6.6	0-28	9.75	-1.01	.77	-2.90,.66	1.17
	WMS-R Visual Repro. II	25.47	10.53	2-41	15.50	-.60	1.49	-3.87,1.62	2.31

Key: BNT-Boston Naming Test, COWAT-Controlled Oral Word Association Test, ANT-Animal Naming Test, WAIS-R- Wechsler Adult Intelligence Scale Revised, GP-Grooved Pegboard, FTT-Finger Tapping Test, D2-Concentration Endurance Test, WCST-Wisconsin Card Sorting Test, RFFT-Ruff Figural Fluency Test, LNS-Letter Number Span Test, WMS-R-Wechsler Memory Scale Revised,
*Note: There are no normative data available for this variable.

FUNCTIONAL DISABILITY

The ratings of functional disability indicated that the participants fell in the moderately to significantly impaired range on the MSIF, the moderately impaired range on the SOFAS and GAF, and the fair to poor range on the SASII (see Table 7). However, the sample does represent a wide range of functioning with some subjects engaging in no productive activity living in a supervised residence and others working full time and living independently with everything in between.

Table 7: Functional Disability Ratings for Participants

Measure	Variable	N	Mean	SD	Range	Inter-quartile
SASII	Role Performance	59[1]	4.27	1.85	1-7	3.00
	Social Leisure	59	4.12	1.54	1-7	2.00
	General Adjustment	59	4.34	1.52	1-7	2.00
MSIF	Global Role Position	60	4.25	1.95	1-7	3.00
	Global Indep. Functioning	60	4.48	1.93	1-7	3.00
DSM-IV	SOFAS	60	55.98	15.17	20-85	29.00
	GAF	60	53.52	15.28	20-85	24.00

[1] one subject was unavailable to complete the SASII

PSYCHOPATHOLOGY

The measure of psychopathology employed in the present study, the BPRS, indicated an overall mild level of psychopathology. Table 8 presents descriptive data regarding the ratings for each of the 18 items of the BPRS, the five BPRS factors, the total BPRS rating, as well as the clinical global impression. Mean level of psychopathology ranged from 1.1 to 2.6 (out of a possible 7, where 1 indicates that the symptom is not present). The range suggests that some patients exhibited more severe symptoms that may have been washed out when averaging across patients and across items. However, this is a sample that is well-maintained on neuroleptics that has mild residual psychopathology.

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Table 8: BPRS Ratings of Item and Factors for Participants (N=60)

BPRS Factor/Item	Mean	SD	Range	Interquartile
Anxiety/Depression Factor (ANDP)	2.08	.84	1-4	1.50
Somatic Concern	1.9	1.3	1-6	2.00
Anxiety	2.6	1.3	1-6	1.75
Guilt Feelings	1.7	1.0	1-4	1.00
Depressive Mood	2.1	1.1	1-4	2.00
Anergia Factor (ANER)	1.83	.74	1-3.5	1.25
Emotional Withdrawal	2.0	1.2	1-5	2.00
Blunted Affect	2.3	1.4	1-6	2.00
Motor Retardation	1.9	1.1	1-5	2.00
Disorientation	1.1	.3	1-2	.00
Thought Disturbance Factor (THOT)	1.79	1.04	1-4.75	1.25
Conceptual Disorganization	1.8	1.2	1-4	2.00
Grandiosity	1.6	1.3	1-6	.00
Hallucinatory Behavior	1.9	1.6	1-6	1.75
Unusual Thought Content	1.8	1.4	1-6	2.00
Activation Factor (ACTV)	1.49	.68	1-3.67	.67
Tension	1.8	1.0	1-4	1.00
Excitement	1.4	.9	1-5	.75
Mannerisms and Posturing	1.3	.6	1-4	.00
Hostility Factor (HOST)	1.93	1.03	1-5.33	1.58
Hostility	1.9	1.3	1-5	2.00
Uncooperativeness	1.8	1.1	1-6	2.00
Suspiciousness	2.1	1.5	1-6	2.00
Total	1.84	.55	1-3.33	.88
Clinical Global Impression	3.0	1.3	1-5	2.00

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ANALYSIS OF THE MAIN HYPOTHESIS: RELATIONSHIP BETWEEN NEUROPSYCHOLOGICAL FUNCTIONING, PSYCHOPATHOLOGY AND FUNCTIONAL DISABILITY

Analysis of the data was accomplished using canonical correlation to examine the association between a set of "explanatory variables" (in this case neuropsychological test scores) and a set of "outcome variables" (in this case measures of functional disability). A principal advantage of canonical correlation over multiple regression analysis is that this technique permits the examination of multivariate associations between two sets of variables and in this case allows for the multidimensional examination of the neuropsychological correlates of disability (Silverstein, Fogg, and Harrow, 1991). Canonical correlation can be considered an extension of factor analysis. In particular, in factor analysis, factors are extracted to explain variance in the same set of variables. In canonical correlation, orthogonal factors, or canonical variates, are formed simultaneously in two sets of variables (set 1 and set 2). The objective here is to obtain as high a correlation as possible between the canonical factor pairs derived form set 1 and 2. Thus orthogonal variates are derived from among the neuropsychological measures and from among the functional disability measures and then the associations between each of the newly derived sets of variates can be determined. Psychopathology as measured by the total rating on the BPRS and the vocabulary subtest score from the WAIS-R were used as covariates in the analysis. This allows a multidimensional approach by determining the relative importance of particular domains of neuropsychological functioning for particular domains of functional disability independent of the level of psychopathology and general verbal intelligence. Table 9 lists

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the variables that were chosen a priori for use in the three sets for the canonical analysis. Note that 59 cases were included in the analysis due to one missing case on the SASII. In spite of a relatively high correlation (NP impairment explained 36% of the variance of the FD measures), the relationship failed to reach significance [R=.63, Wilks' Lambda=.25, df1=70, df2=240, p=.63]. The analysis was repeated with men only (N=45) to determine whether the skewed distribution of gender was a factor. The results were also not significant [R=.67, p=.80].

Table 9: List of Variables Used For the Main Statistical Analysis

Set	Variables
Explanatory Set-NP Measures	
Language	BNT Total Correct COWAT Total Correct
Motor	GP Non-Dominant Time FTT Dominant Time
Executive	WCST Perseverative Errors RFFT Perseverative Error
Attention	LNS Total Correct D2 Errors
Memory	WMS-R Logical Memory I WMS-R Visual Reproduction I
Set of Covariates	WAIS-R Vocabulary BPRS Total
Outcome Set-FD Measures	SASII Instrumental Role Functioning Global SASII Social Leisure Global SASII General Adjustment Global MSIF Role Position Global MSIF Independent Functioning Global GAF SOFAS

*Note: N=59 due to one missing case on the SASII.

SECONDARY ANALYSES

Although the analysis of the main hypothesis did not reveal a statistically significant relationship between the set of NP and FD measures, it is conceivable that such a relationship exists but that the model chosen to analyze the relationship on an a-

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priori basis was not appropriate to the task. First, additional analyses were completed to determine if there were factors that interfered with the main analysis. Then, additional canonical correlation analyses were conducted to further explore the inter-relationships between NP, PY and FD measures.

Principal Component Analysis

A principal component analysis was completed for the explanatory and outcome set used in the canonical correlation described above to determine whether the a-priori choice of variables was valid. For the explanatory set (the neuropsychological test scores), the unrotated solution produced a general factor that explained 32.6% of the variance. To look at the components, a rotated factor structure was extracted. Four factors were revealed that met the criteria of having explained a significant portion of the variance (eigenvalue greater than one). The factor loadings are presented in Table 10. The memory, motor, language and executive variables were separate factors. This suggests that the a-priori domain selections of the neuropsychological variables from the literature were valid.

Table 10: Rotated Factor Loadings of the Explanatory Set of NP Variables (N=60)

NP Variables	Factor 1	Factor 2	Factor 3	Factor 4
BNT Total Correct			.69	
COWAT Total Correct			.86	
GP Non-Dominant Time		-.75		
FTT Dominant Time		.88		
WCST Perseverative Errors				
RFFT Perseverative Error				.93
LNS Total Correct				
D2 Errors				
WMS-R Logical Memory I	.72			
WMS-R Visual Reproduction I	.82			

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The unrotated solution for the outcome set also produced a general factor that explained 74 % of the variance. The results for the rotated analysis revealed three factors (see Table 11). These findings suggest that there are distinct dimensions in the outcome set such that the SASII social leisure rating, MSIF global ratings and the DSM-IV (GAF/SOFAS) global ratings are separate factors that measure functional disability in different ways. This supports the choice of rating scales, however, the fact that the general factor explains such a large portion of the variance indicates that there is a lot of overlap. This provided a guide for the choice of variables for the secondary analyses described below.

Table 11: Rotated Factor Loadings of the Outcome Set of FD Variables (N=60)

FD Variables	Factor 1	Factor 2	Factor 3
SASII Instrumental Role Functioning Global			
SASII Social Leisure Global			.98
SASII General Adjustment Global			
MSIF Role Position Global	.91		
MSIF Independent Functioning Global	.91		
GAF		.87	
SOFAS		.79	

Correlations Between Illness Chronicity and Severity Variables and Neuropsychological Performance, Psychopathology, and Functional Disability Variables

Correlational analyses were completed to determine whether there were any relationships between illness severity variables and NP, PY and FD variables. Any significant demographic or illness severity variable would then be used as a covariate in secondary analyses. The illness chronicity and severity (ICS) variables included age, age of onset of treatment, medication dose, time since onset of treatment, time since

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hospitalization, duration of most recent hospitalization, and total number of lifetime hospitalizations.

No significant relationship was seen between the 10 neuropsychological variables used in the main analysis and the ICS variables with one exception. Total number of hospitalizations was correlated with WMS-R Visual Reproduction performance (r=-.27, p=.04) such that worse performance on this visual memory test was seen in patients with more hospitalizations.

No significant relationship was seen between the functional disability ratings used in the main analysis and age, time since last hospitalization, total number of hospitalizations, time since onset of treatment, or duration of the last hospitalization. Age of onset of treatment was significantly related to the MSIF Global Role Position and Global Independent Functioning (r=-.30, p=.02; r=-.31, p=.02) such that those with an earlier onset performed worse on these measures than those with later onsets. Current dose of medication was significantly correlated with GAF ratings (r=-.30, p=.02) such that subjects with higher doses received worse GAF ratings.

BPRS factors from the main analysis were not correlated with age, total number of hospitalizations, duration of the most recent hospitalization or time since the most recent hospitalization. Current medication dose was significantly related to BPRS Thought Disturbance, Activation, and Hostility Factors (r=.36, p=.005; r=.29, p= .027; r=.27,p= .034 respectively). The Hostility factor was also significantly related to the subjects' age of onset of treatment (r=-.27, p=.035) and time since the onset of treatment (r=.26, p=.05) such that those with earlier onsets and more time since the onset of treatment had higher ratings of psychopathology.

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Since one would expect one out of 20 correlations to be significant at random given a p value of .05, the finding of 9 significant correlations out of 154 performed (10 NP variables, 7 FD variables, 5 PY variables by 7 ICS variables) suggests that these associations may have occurred by chance. Therefore, the ICS variables were not used as covariates in the secondary analyses.

Canonical Correlations between NP Performance and Functional Disability

Five canonical correlations were conducted to examine the relationship between each domain of NP functioning and FD. Four variables were used in the predictor and outcome sets. The number of variables included was chosen in order to increase the amount of explained variance while keeping the number low due to the variable to case ratio. The choice of variables was based on the principal component analysis (PCA) described above. The PCA revealed that the *a-priori* choice of NP variables for the primary analysis was valid, that is, the variables seem to measure the intended domain. Therefore, the same two variables in each domain that were used in the primary analysis were used again in the secondary analyses with an additional two variables chosen for each domain (as seen in Table 12).

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Table 12: List of NP Variables Used For the Secondary Statistical Analyses (N=60)

NP Domain	Variable
Language	BNT Total Correct
	COWAT Total Correct
	ANT Total Correct
	WAIS-R Vocabulary
Motor	GP Non-Dominant Time
	FTT Dominant Time
	D2 Total Letters
	WAIS-R Digit Symbol
Executive	WCST Perseverative Errors
	WCST Categories
	RFFT Perseverative Error
	RFFT unique designs
Attention	LNS Total Correct
	WMS-R Visual Span Backward
	WMS-R Digits Backward
	D2 Errors
Memory	WMS-R Logical Memory I
	WMS-R Visual Reproduction I
	WMS-R Logical Memory II
	WMS-R Visual Reproduction II

The reduction of the number of variables in the outcome set of functional disability measures to four was consistent with the findings of redundancy on the PCA. The choice of variables was also based on the PCA. The SASII Instrumental Role Performance and General Adjustment Ratings were dropped as they were not contributing to the model. They are also highly correlated with the MSIF variables. The GAF was also dropped as it incorporates psychopathology in the rating. The SOFAS is a purer measure of FD and it also loaded highly in the PCA. Table 13 presents the four variables chosen for use in the secondary canonical correlations.

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Table 13: List of FD Variables Used For the Secondary Statistical Analyses (N=60)

FD Measure	Variable
MSIF	Role Position Global
MSIF	Independent Functioning Global
SASII	Social Leisure Global
DSM-IV	SOFAS

The canonical correlations between each of the 5 NP domains and FD revealed no significant relationships between memory, language, motor, or executive with FD. There was a significant relationship found between Attention and FD (R=.58, p=.00). The standardized canonical coefficients derived for the FD measures were loaded highly with MSIF Role Position Global and MSIF Independent Functioning Global (with opposite signs). The canonical variates derived for the Attention measures were loaded highly with Letter Number Span Total Correct and WMS-R Digit Span Backwards (see Table 14). A non-significant trend was seen when this analysis was repeated with men only. [R=.46, p=.09].

Table 14: Standardized Canonical Coefficients for Attention-Functional Disability Analysis

Explanatory Set-Attention		Outcome Set-FD	
Variable	**Coeff.**	**Variable**	**Coeff.**
D2 Total Errors	.31	MSIF Role Position Global	2.26
WMS-R Visual Span Backwards	.44	MSIF FD Global	-2.60
WMS-R Digits Backwards	-.62	SASII Social Leisure Global	.54
LNS Total Correct	.89	SOFAS	.63

Canonical Correlation between Psychopathology and Functional Disability

A canonical correlation was completed with psychopathology ratings (BPRS Factors as described on pg. 67) as the predictor set and FD as the outcome set (see Table 15).

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Table 15: Variables Used in Canonical Correlation between Psychopathology and FD

Explanatory Set-Psychopathology Ratings	Outcome Set-Indep. Functioning
BPRS Anxiety and Depression Factor (ANDP)	MSIF Role Position Global
BPRS Anergia Factor (ANER)	MSIF Indep. Functioning Global
BPRS Thought Disturbance Factor (THOT)	SASII Social Leisure Global
BPRS Activation Factor (ACTV)	DSM-IV SOFAS
BPRS5 Hostility and Suspiciousness (HOST)	

The results were suggestive of a relationship but did not reach statistical significance (R=.54, p=.08). The canonical variates derived for the PY measures were loaded highly with BPRS Anergia Factor and BPRS Thought Disturbance Factor. The canonical variates derived for the FD measures were loaded highly with SOFAS and SASII Social Leisure (see Table 16). When reanalyzed with men only, the results were not significant [R=.55, p=.49].

Table 16 : Standardized Canonical Coefficients for the Psychopathology-Functional Disability Analysis

Explanatory Set-PY		Outcome Set-FD	
Variable	**Coefficient**	**Variable**	**Coefficient**
BPRS-ANDP	.05	MSIF Role Position Global	.17
BPRS-ANER	.69	MSIF FD Global	.03
BPRS-THOT	.62	SASII Social Leisure Global	.30
BPRS-ACTV	-.06	SOFAS	-.68
BPRS-HOST	.18		

Canonical Correlations between Neuropsychological Performance and Psychopathology

Canonical correlations were conducted with the five BPRS factors and each of the 5 NP domains. No significant associations were observed.

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Canonical Correlations between Current Neuropsychological Performance, Current Psychopathology, and Past Functional Disability

In order to determine whether the lack of significance of the main analysis was due to its cross-sectional nature, the above analyses were repeated measures of past functional disability as the outcome set. Disability is difficult to measure when sampling from only one time point. For example, some patients may have just gotten a job that they lost the following week while others might be scheduled to attend school the following fall. The following analyses used data collected regarding the subjects' activity over the past five years to capture a history of disability. Four variables were used to capture FD over the past five years: total days hospitalized, number of hospitalizations, number of months worked (at any salary and for any number of hours per week), and a weighted composite variable of productive activity. This last variable was created by developing a hierarchy of activities (based on quantity and quality of the activity), multiplying the number of months engaged in each of these activities by its given weight, and summing the results (see Table 17).

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Table 17: Productive Activity over Past Five Years Calculation

# of months in each Activity	weight/multiplier
Work at Paid Job above minimum wage-Full Time	24
Work at Paid Job above minimum wage-Half Time	23
Work at Paid Job above minimum wage-Part Time	22
Work at Paid Job at/below minimum wage-Full Time	21
Work at Paid Job at/below minimum wage-Half Time	20
Work at Paid Job at/below minimum wage-Part Time	19
Work at Volunteer Job-Full Time	18
Work at Volunteer Job -Half Time	17
Work at Volunteer Job -Part Time	16
Mainstream College -Full Time	15
Mainstream College -Half Time	14
Mainstream College -Part Time	13
Certificate/Trade School -Full Time	12
Certificate/Trade School -Half Time	11
Certificate/Trade School -Part Time	10
Non-Mainstream Vocational Training -Full Time	9
Non-Mainstream Vocational Training -Half Time	8
Non-Mainstream Vocational Training -Part Time	7
Pre-Vocational Rehabilitation -Full Time	6
Pre-Vocational Rehabilitation -Half Time	5
Pre-Vocational Rehabilitation -Part Time	4
Psychosocial Club -Full Time	3
Psychosocial Club -Half Time	2
Psychosocial Club -Part Time	1

Five canonical correlations were conducted with each of the five NP domains (see Table 12, page 74) in the predictor set and past functional disability (PFD) variables in the outcome set. No relationship was found between the NP domains of memory, language, motor or attention and past five-year activity. Results for the executive domain were suggestive of a relationship to past five year functional disability but did not reach statistical significance [R=.47, p=.06]. The canonical variates derived for the Executive measures were loaded highly with WCST Perseverative Errors and Categories. The canonical variates derived for the PFD measures were loaded highly with all four

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variables (see Table 18). The results achieved statistical significance when the sample was reduced to only men [R=.52, p=.02].

Table 18: Standardized Canonical Coefficients for the Executive-Past Functional Disability Analysis

Explanatory Set-Executive		Outcome Set-PFD	
Variable	**Coefficient**	**Variable**	**Coefficient**
WCST Perseverative Errors	1.04	Productive Activity	1.53
WCST Categories	1.02	Total Days in Hosp	-1.65
RFFT Perseverative Error	.42	# of hospitalizations	1.36
RFFT unique designs	-.67	Months Worked	-1.63

A canonical correlation was conducted with the PY ratings (5 BPRS factor scores) in the predictor set and past functional disability in the outcome set. A significant relationship was seen between PY and past five year activity (R=.58, p=.007). The canonical variates derived for the PY measures were loaded highly with BPRS Anergia Factor and BPRS Activation Factor. The canonical variates derived for the PFD measures were loaded highly with productive activity and work (see Table 19). The results remained significant when the sample was reduced to only men [R=.61, p=.03].

Table 19: Standardized Canonical Coefficients for the Psychopathology-Past Functional Disability Analysis

Explanatory Set-PY		Outcome Set-PFD	
Variable	**Coefficient**	**Variable**	**Coefficient**
BPRS-ANDP	.40	Productive Activity	-2.17
BPRS-ANER	.64	Total Days in Hosp	.24
BPRS-THOT	-.14	# of hospitalizations	.15
BPRS-ACTV	-.54	Months Worked	2.19
BPRS-HOST	.27		

Summary

Table 20 presents a summary of the results of the canonical correlational analyses.

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Table 20: Summary of the Canonical Correlational Analyses Results

Explanatory Set	Outcome Set	Canonical Correlation	Explanatory Set Variables Accounting for the Most Variance	Outcome Set Variables Accounting for the Most Variance
Neuropsychological Functioning (5 domains) covariates=Psychopathology and Verbal Intelligence	Functional Disability (FD)	NS		
Attention	FD	R=.58 p.00	+ Letter Number Span - WMS-R Digits Backward	- MSIF Global FD + MSIF Global Role Position
Language	FD	NS		
Motor	FD	NS		
Executive	FD	NS		
Memory	FD	NS		
Psychopathology	FD	R=.54 p.08	+ BPRS Anergia Factor + BPRS Thought Factor	- SOFAS + SASII Social Leisure
Attention	Psychopathology	NS		
Language	Psychopathology	NS		
Motor	Psychopathology	NS		
Executive	Psychopathology	NS		
Memory	Psychopathology	NS		
Executive	Past Functional Disability(PFD)	R=.47 p=.06	+ WCST Categories +WCST Perseverative Errors	+ Productive Activity - Days Hospitalized + Number of Hospitalizations - Months Worked
Attention	PFD	NS		
Language	PFD	NS		
Motor	PFD	NS		
Memory	PFD	NS		
Psychopathology	PFD	R=.58 p=.007	+ BPRS Anergia Factor - BPRS Activation Factor	- Productive Activity + Months Worked

Key: WCST=Wisconsin Card Sorting Test, BPRS=Brief Psychiatric Rating Scale, WMS-R=Wechsler Memory Scale-Revised, MSIF=Multidimensional Scale of Independent Functioning, SOFAS=Social and Occupational Functioning Assessment Scale, SASII=Social Adjustment Scale II

DISCUSSION

Overall, the results lend some support to the hypotheses that NP performance would correlate with FD independent of psychopathology and that NP performance and psychopathology would relate to different aspects of functional disability.

DESCRIPTION OF THE SAMPLE

There was measurable neuropsychological impairment across all domains tested in the study sample. While this is not a surprising finding based on the recent literature, it highlights how far the role of neuropsychology in psychiatric disorders has come. Not long ago neuropsychologists were asked to "rule out organicity" by using neuropsychological testing to confirm the diagnosis of psychiatric disorders including schizophrenia. It was felt that SZ was a functional disorder that did not affect the brain. There is now a consensus that NP deficits are not only present in SZ, but that they are severe and persistent. However, the consequences of these deficits are still relatively unknown.

The sample reflected a wide range of functional disability levels that averaged in the moderately disabled range. While functional disability is described in the literature, it is mostly discussed in terms of "outcome". This usually refers to how much time a patient is in the hospital or whether or not they are employed. Many investigators examine functional disability while the patient is in the hospital or assess only circumscribed areas of functioning. Few look at a range of functioning in the community. This study employed a sample of patients living in the community engaged in a range of activities. Many lived at home with their families or in a supportive housing program, while some lived on their own. Some worked competitively, some in

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supportive employment programs and yet others had volunteer positions. Many attended vocational training or rehabilitation programs while a few were even in college. Some were not able to engage in any activities. The measures used in this study were designed to capture this range of functioning in the community. An improved understanding of what impedes these patients from living on their own or sustaining employment is crucial. Not only would it enhance clinicians' abilities to work with these patients, it may lead to better treatments, and it may help reformulate a more valid nosology of the illness.

The level of psychopathology in the group fell in the mild range. This study was designed to assess a sample of outpatients with a range of functional disability. It was successful in that respect and these patients show only mild residual psychopathology. All patients in the sample were taking antipsychotic medication that aimed at minimizing their psychopathological symptoms. However, they remained functionally disabled. This study's goal was to understand why these patients who are not acutely psychotic are so disabled. It was hypothesized that the pervasive neuropsychological impairment seen in these patients would significantly contribute to their ability to function independently in the community.

PRIMARY ANALYSIS

The primary analysis was designed on an a-priori basis to examine the contribution of NP impairment to functional disability. It was important to eliminate any contribution that psychopathology and IQ might have to functional disability. Therefore, a canonical correlation was conducted with 10 neuropsychological variables (2 for each of 5 domains: memory, attention, executive, language and motor) in the predictor set and

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7 functional disability variables in the outcome set with a ratings of overall psychopathology and verbal IQ as covariates. This analysis, while not reaching statistical significance, revealed a relatively high correlation. Therefore, strictly speaking, the hypothesis was not confirmed. However, the magnitude of the association was high enough to be compelling and warranted further exploration.

One possible reason for the lack of a significant finding is that the a-priori choice of variables was inappropriate. It was important to determine whether the variables chosen to represent the five domains of neuropsychological functioning actually did so. It was also necessary to see if the functional disability measures used in the analyses captured different aspects of functional disability. To confirm the choice of variables in the main analysis, principle component analyses (PCA) of the predictor and outcome sets were completed. The PCA of the neuropsychological variables revealed that the a-priori domain selections of the neuropsychological variables from the literature were valid. The PCA of the functional disability variables suggested that distinct dimensions of functioning were assessed, however, there was significant redundancy of measurement. These results were used to determine the variables used in the secondary canonical correlations to further explore the relationships between neuropsychological performance, psychopathology and functional disability.

Another concern was that potentially confounding illness chronicity and severity (ICS) variables were not accounted for in the main analysis. The particular variables of concern were age, age of onset of treatment, medication dose, time since onset of treatment, time since hospitalization, duration of most recent hospitalization, and total number of lifetime hospitalizations. These ICS variables could be related to functional

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disability while the analysis was attempting to determine the separate contribution of neuropsychological impairment to functional disability. For example, patients in the sample who are older or have been sick longer may be more impaired and functionally disabled than younger patients who are early in the course of the illness. The consequences of neuropsychological impairment might be different for patients with different levels of illness severity or lengths of illness. Correlational analyses were completed to determine whether there were any relationships between ICS variables and NP, PY and FD variables that needed to be accounted for in the secondary analyses. The results of the analyses suggested that illness severity and chronicity was not significantly associated with the measures of functional disability, NP performance or psychopathology. Therefore, ICS variables did not need to be introduced into the secondary analyses.

Another possible reason that the primary analysis did not reach significance is that there was not enough power. Although the sample size was relatively large, the primary analysis was comprised of a large number of variables with substantial variability.

SECONDARY ANALYSES

The secondary analyses were comprised of a series of canonical correlations designed to examine the separate contributions of neuropsychological impairment and psychopathology to functional disability. The variables used in the analyses were determined from the results of the PCA analyses described above in order to maximize the amount of explained variance. The number of variables in each analysis, the variability of the explanatory set, and the redundancy of the outcome set were all reduced.

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Canonical Correlations between NP Performance and Functional Disability (FD)

Five canonical correlations were performed to separately examine the contributions of each of the five domains of neuropsychological functioning to functional disability. Attention was the only domain that was significantly related to FD. In order to interpret the canonical correlation, the signs of the canonical coefficients needs to be considered. As Letter Number Span and WMS-R Digits Backwards are both scaled the same way such that high scores reflect better performance, the opposite signs of the canonical weights indicates that it is a difference in performance on these two tests that is related to the measures of functional disability. One interpretation is that this reflects the added difficulty inherent in the Letter Number Span Test when compared to the WMS-R Digit Span Subtest. LNS may have more demand on working memory and some patients may do well on the Digit Span subtest but not on Letter Number Span.

Similarly, the opposite signs of the canonical weights for MSIF Global Role Position and Global Independent Functioning variables (which are both rated on the same scale) signifies that it is the difference between these ratings that is related to the predictor set. This may be interpreted as reflecting the impact of the level of support used and performance difficulties for the given role position. For example, someone that receives a rating of 4 for global role position but needs no support and is having no performance problems will receive a 4 for the global independent functioning rating. Someone else with a role position rating of four but who is having either difficulties in their role or needs a lot of support would receive a higher rating on the global independent functioning rating.

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Thus, looking at the whole model, the results suggest that the working memory aspect of the attention measures was related to a difference between the subjects MSIF Role Position and Independent Functioning Ratings which reflects the contribution of support required and or performance deficits. In other words, subjects requiring support or having difficulty in their role responsibilities (including vocational, educational and residential domains) had more severe working memory deficits. This finding makes intuitive sense since complex attention skills (such as doing two things at once, holding instructions in mind while working on a task, and switching back and forth between two tasks) are necessary for any work, education or living role. Patients with SZ also demonstrate increased impairment with increased attentional demand.

These findings are consistent with the literature as several studies have found relationships between impairments in attention and global independent functioning (Goldberg et al., 1990), vocational disability (Goldman et al. 1998) and residential functioning (Wykes, Sturt, and Katz, 1990). It is surprising that other NP domains, especially executive functioning were not related to FD given the findings in the literature. However, Gold et al. (1997) found that impaired performance on the WCST might reflect a working memory deficit. Also, it is possible that the cross-sectional nature of the analysis impeded the ability to see the relationship.

Canonical Correlation between Psychopathology and Functional Disability

The canonical correlation between Psychopathology and FD revealed a trend toward a relationship that did not quite reach significance. No significant relationship was observed when only men were analyzed.

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In this case, the BPRS Anergia and Thought Disorder factors in the predictor set have positive coefficients and are rated on the same scale, thus, having high ratings on both factors or low ratings on both factors is related to the outcome set.

The difference in sign of the coefficients for the SASII Social Leisure and SOFAS reflects the opposite scaling of the measures. Therefore, high levels of psychopathology are related to impaired social functioning. This suggests that increased thought disturbance and anergia negatively affects a subject's ability to interact socially. It makes sense that if a patient has difficulties engaging in activities or communicating with others that their ability to interact socially with others would be affected.

While the finding was not predicted, supporting evidence is found in the literature that negative symptoms are correlated with social disability (Bellack et al., 1989; Morrison et al., 1990). Thought disturbance has also been shown to impact communication skills that are crucial for social competence (Baltaxe & Simmons, 1995).

Canonical Correlations between Neuropsychological Performance and Psychopathology

No significant relationships were found between any of the NP domains and the five BPRS factors. While this finding may seem counterintuitive, the independence of psychopathological symptomatology and NP impairment has been consistently found in the literature e.g. (Bellack et al., 1990a; Strauss & Carpenter, 1972; Strauss & Carpenter, 1978; Strauss et al., 1974). This suggests that NP impairment and psychopathology may be distinct manifestations of the illness that affect patients in different ways.

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Canonical Correlations between Neuropsychological (NP) Performance and Past Functional Disability (PFD)

Another possible reason that the main analysis did not reach significance could be the cross-sectional nature of the analysis. In an attempt to examine the NP contribution to history of functional disability, retrospective data from patient self-report, chart reviews and other sources (such as family or health professionals) was collapsed into four variables that captured functional disability over the past five years. Five canonical correlations were then completed to analyze the relationship between each of the five domains of current NP performance and past functional disability.

A trend toward a relationship between executive functioning and PFD was observed that did reach significance when looking at men only. WCST Categories and Perseverative Errors were the highest loading coefficients from the predictor set and both had positive coefficients. This means that scores in the same direction on both are related to the outcome set. However, the Categories variable is scaled such that high scores reflect better performances while the perseverative errors variable is scaled so high scores reflect poor performance. Although they are negatively correlated with each other it is possible to have high scores on both or low scores on both. Given the characteristics of the WCST, it is possible to complete a low number of categories with a low number of perseverative errors when a high number of non-perseverative errors are made. Also, one can complete a high number of categories but take all 128 cards and make a high number of perseverative errors.

All four variables in the outcome set had high-loading coefficients. The productive activity and months work variables are based on the same scale where high

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ratings reflect better functioning. The opposite signs of these variables indicate that a difference in the ratings on these variables is related to the predictor set. Given the way the scale is designed (see Table 17 pg. 78) one can have a high score on past productive activity even if they did not work since they may have participated in educational, vocational or rehabilitative programs. The other two variables in the outcome set (number of hospitalizations and number of days hospitalized) also have oppositely signed coefficients although they are scaled in the same direction. This means that a difference in the score on these variables is related to the predictor set. This could mean a high number of hospitalizations with a short total duration or low number of hospitalizations with a high total duration.

Summarizing the whole model, the relationship between executive functioning and past functional disability is maximal with particular patterns of performance on the WCST (categories and perseverative errors both high or both low) of activity (low work with possibly high training and rehabilitation) and of hospitalization (frequent short stays and infrequent long stays). A significant relationship between executive functioning, particularly performance on the WCST, and vocational functioning has been demonstrated in several studies (Berns et al., 1995; Lysaker, Bell, and Beam Goulet, 1995; Meltzer et al., 1996). It seems reasonable that executive functions such as the ability to monitor one's behavior, take feedback, and problem solve would be crucial for success in any work, education, or living environment.

Canonical Correlation between Psychopathology and Past Functional Disability

A canonical correlation was then completed to analyze the relationship between current psychopathology and functional disability over the past five years.

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Psychopathology was significantly related to past functional disability. The anergia and activation factors had high loading coefficients of opposite signs although they are rated on the same scale. This indicates that a difference in the ratings on these variables is related to the outcome set. Given the opposite nature of these variables it is most likely reflecting high levels of anergia and low levels of activation.

Productive activity and work are the highest loaded measures in the outcome set with coefficients of opposite sign. As described above this may reflect use of rehabilitation and training programs.

Therefore, the findings of this model suggest that subjects with more negative symptoms worked less and utilized more training and rehabilitation services. The fact that negative symptoms explained 34% of the variance despite the reduced range of psychopathology in this sample gives strong support to previous studies providing evidence that negative symptoms are related to functional disability (i.e. Breier et al., 1991; Corrigan et al., 1994). This is not surprising since negative symptoms are the more enduring aspects of the illness not impacted significantly by neuroleptic medication.

Summary

While the primary analysis did not reach statistical significance, the magnitude of the association was high enough to warrant further exploration. Cross-sectional analyses indicated that one domain of neuropsychological functioning (namely attention) was related to vocational disability while psychopathology (particularly anergia and thought disturbance) was related to social disability. Analyses of the relationship between current NP performance and history of FD revealed a trend towards a relationship between executive functioning and past functional disability. A robust relationship was observed

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between current PY ratings (particularly negative symptoms) and different aspects of past functional disability. No relationship was found between neuropsychological functioning and psychopathology. These findings modestly support the hypotheses that severity of neuropsychological deficits would be correlated with functional disability independent of psychopathological symptomatology and that NP deficits and PY ratings would be correlated with different aspects of functional disability.

Limitations and Future Directions

This study had several limitations including its relatively small case to variable ratio, skewed gender distribution, and cross-sectional nature. The reduced range of psychopathology observed in this sample and the exclusion of inpatients may also be seen as a limitation. The interpretation of the data is not intended to suggest that acute psychopathology is irrelevant. However, it is striking that these "success stories", that is, patients who are relatively stabilized on medication with few residual symptoms who receive at least some mental health services are so functionally disabled. This sample does represent a large portion of the SZ patients in the community that are still struggling to live more independently (Velligan et al., 1997).

The strong association between negative symptoms and functional disability despite the reduced range of negative symptoms highlights the need for more research in this area toward the development of targeted treatments of this enduring aspect of the illness. Better measurement of negative symptoms is needed as well as a greater appreciation and understanding of the chronic role they play in the illness. Negative symptoms often do not respond to current neuroleptic medication and are therefore targets for new pharmacotherapeutic and rehabilitative efforts.

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The lack of appreciation of the NP impairment in SZ has led to missed treatment opportunities. The pervasive NP impairment is not considered in treatment planning (Jaeger & Douglas, 1992; Malla et al., 1997). Patients are often believed to be unmotivated when they have trouble sustaining a job or independent living situation. (Anthony et al., 1990) However, their NP impairment may be a barrier to developing the necessary skills for such roles. This highlights the need to establish the efficacy of NP informed treatment techniques for use in this population. Cognitive remediation is a widely accepted form of treatment for patients with head injuries and other neurological illnesses (Diller, 1987). Recently, several studies have reported promising findings for the use of such methods in SZ (Cassidy, Easton, Capelli, Singer, and Bilodeau, 1996; Green, 1993; Spring & Ravdin, 1992; Stuve, Erickson, and Spaulding, 1991). However, studies with more rigorous methodology are needed to establish the efficacy and effectiveness of cognitive remediation in patients with SZ (Hogarty & Flesher, 1992; Spaulding, 1992). Increased appreciation of the relevance of NP impairment in SZ may also help develop new strategies for the early diagnosis of SZ possibly even before the first manifestation of a psychosis (Weinberger & Gallhofer, 1997). There has also been recent effort to measure the efficacy of new drug treatments for SZ on not only psychopathology, but also neuropsychological impairment (Meltzer, 1992). Buchanan and Carpenter (1997) suggest that increased understanding of the independence of different symptom complexes of SZ (such as neuropsychological impairment and psychopathology) may be critical for studying the underlying neuropathophysiology.

While the findings are preliminary, they show the importance of studying schizophrenia in a multidimensional fashion and highlight the need for prospective,

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longitudinal studies that assess large numbers of subjects at all phases of illness to further elucidate the inter-relationships between psychopathology, NP impairment and functional disability. The understanding of these relationships may provide a guide for the development of more effective interventions and supports as well as provide clues for the development of a more reliable nosology of SZ.

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APPENDIX

Informed Consent to Participate in:

Neuropsychological Deficits and Functional Disability in Patients with Schizophrenia

Expected Duration of the Subject's Participation:

Your participation in this study may take up to 8 hours in as many sessions as needed.

Purpose of this Project:

This study examines the relationship between cognition (which includes memory, problem solving, attention) and independent living skills (which includes working, school, and living responsibilities) in patients with schizophrenia.

Description of Procedures:

You will be administered pencil and paper tests that assess skills such as memory, attention and problem solving. During some of these tasks you will be timed. You also will be asked questions about any symptoms you may have experienced during the past week as well as questions about work, education and living arrangements. If you become tired you may ask for a break or request that testing be continued on another day.

Possible Discomforts and/or Risks:

Potential risks of participating in this study are extremely minimal but may include fatigue and test anxiety.

Possible Benefits of Participation:

Potential benefits of participating in this study may include the advantage of careful monitoring of your condition and circumstances.

Alternative Treatment Available:

Although this study does not involve a treatment, you have the alternative of not taking part in the study. Your decision to take participate is voluntary. Your identity and participation are confidential to the extent permitted by law. Your test results will not be identified with your name, but by a number code to maintain your confidentiality and all results will be stored in locked areas. If you decide not to participate or if you choose to withdraw after beginning the study, you will not lose any benefits associated with your medical care. You are encouraged to ask questions before deciding whether you wish to participate and any time during the course of the project by contacting Stefanie Berns at

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718-470-8436 or Dr. Jaeger, the Director of Neuropsychological Rehabilitation Research at 718-470-8342. For questions concerning this research project and/or research subjects' rights, you should call the Office of Research Services at 516-326-7658. A copy of this consent will be given to you.

I hereby consent to participate.

Subject's Name (print)	Witness Signature (someone with no connection to this research project)
Subject's Signature	Witness Identification (nurse, friend, receptionist, etc.)
Date	

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REFERENCES

Addington, J., Addington, D., & Maticka-Tyndale, E. (1991). Cognitive functioning and positive and negative symptoms in schizophrenia. Schizophrenia Research, 5(2), 123-134.

Affleck, J.W., & McGuire, R.J. (1984). The measurement of psychiatric rehabilitation status: A review of the needs and a new scale. British Journal of Psychiatry, 145, 517-525.

Albee, G.W., Lane, E.A., & Reuter, J.M. (1964). Childhood intelligence of future schizophrenics and neighborhood peers. Journal of Psychology, 58(1), 141-144.

Allebeck, P. (1989). Schizophrenia: A life-shortening disease. Schizophrenia Bulletin, 15(1), 81-89.

American Psychiatric Association. (1980). Diagnostic and Statistical Manual of Mental Disorders (DSM-III). (Third ed.). Washington,D.C.: American Psychiatric Association.

American Psychiatric Association. (1994). Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). (Fourth ed.). Washington, DC: American Psychiatric Association.

Anderson, C.A., Reiss, D.J., & Hogarty, G.E. (1986). Schizophrenia and the Family. New York: Guilford Press.

Andreasen, N.C. (1981). Scale for the Assessment of Negative Symptoms (SANS). Iowa City: University of Iowa.

Andreasen, N.C. (1982). Negative symptoms in schizophrenia: Definition and reliability. Archives of General Psychiatry, 39, 784-788.

Andreasen, N.C. (1985). Positive vs. negative schizophrenia: A critical evaluation. Schizophrenia Bulletin, 11(3), 380-389.

Andreasen, N.C. (1987). The diagnosis of schizophrenia. Schizophrenia Bulletin, 13(1), 9-22.

Andreasen, N.C. (1997). The evolving concept of schizophrenia: From Kraepelin to the present and future. Schizophrenia Research, 28, 105-109.

Andreasen, N.C., Flaum, M., Swayze, V.W., Tyrrell, G., & Arndt, S. (1990). Positive and negative symptoms in schizophrenia: A critical reappraisal. Archives of General Psychiatry, 47(7), 615-621.

Andreasen, N.C., Rezai, K., Alliger, R., Swayze, V.W., Flaum, M., Kirchner, P., Cohen, G., & O'Leary, D.S. (1992). Hypofrontality in neuroleptic-naive patients and in

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patients with chronic schizophrenia. Assessment with xenon 133 single- photon emission computed tomography and the Tower of London. Archives of General Psychiatry, 49, 943-958.

Andrews, G., Hall, W., Goldstein, G., Lapsley, H., Bartels, R., & Silove, D. (1985). The economic costs of schizophrenia: Implications for public policy. Archives of General Psychiatry, 42, 537-543.

Anthony, W.A., Cohen, M., & Farkas, M.D. (1990). Psychiatric Rehabilitation. Boston: Center for Psychiatric Rehabilitation.

Anthony, W.A., & Jansen, M.A. (1984). Predicting the vocational capacity of the chronically mentally ill: Research and policy implications. American Psychologist, 39(5), 537-544.

Anthony, W.A., & Liberman, R.P. (1986). The practice of psychiatric rehabilitation: Historical, conceptual, and research base. Schizophrenia Bulletin, 12(4), 542-559.

Anthony, W.A., Rogers, E.S., Cohen, M., & Davies, R.R. (1995). Relationships between psychiatric symptomatology, work skills, and future vocational performance. Psychiatric Services, 46, 353-358.

Aro, S., Aro, H., & Keskimaeki, I. (1995). Socio-economic mobility among patients with schizophrenia or major affective disorder: A 17-year retrospective follow-up. British Journal of Psychiatry, 166(6), 759-767.

Attkisson, C., Cook, J.A., Karno, M., Lehman, A., McGlashan, T.H., Meltzer, H.Y., O'Connor, M., Richardson, D., Rosenblatt, A., Wells, K., Williams, J., & Hohmann, A.A. (1992). Clinical services research. Schizophrenia Bulletin, 18, 561-626.

Baltaxe, C.A., & Simmons, J.Q.I. (1995). Speech and language disorders in children and adolescents with schizophrenia. Schizophrenia Bulletin, 21(4), 677-692.

Barr, W.B., Bilder, R.M., Goldberg, E., Kaplan, E., & Mukherjee, S. (1989). The neuropsychology of schizophrenic speech. Journal of Communication Disorders, 22(5), 327-349.

Baser, C.A., & Ruff, R.M. (1987). Construct validity of the San Diego Neuropsychological Test Battery. Archives of Clinical Neuropsychology, 2, 13-32.

Becker, D.R., & Drake, R.E. (1994). Individual placement and support: A community mental health center approach to vocational rehabilitation. Community Mental Health Journal, 30(2), 193-206.

Beiser, M., Bean, G., Erickson, D., Zhang, J., Iacono, W.G., & Rector, N.A. (1994). Biological and psychosocial predictors of job performance following a first episode of psychosis. American Journal of Psychiatry, 151(6), 857-863.

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Bell, M., Milstein, R., Beam, G.J., Lysaker, P., & Cicchetti, D. (1992). The Positive and Negative Syndrome Scale and the Brief Psychiatric Rating Scale: Reliability, comparability, and predictive validity. Journal of Nervous and Mental Disease, 180(11), 723-728.

Bellack, A.S., Morrison, R.L., Mueser, K.T., & Wade, J.H. (1989). Social competence in schizoaffective disorder, bipolar disorder, and negative and non-negative schizophrenia. Schizophrenia Research, 2, 391-401.

Bellack, A.S., Morrison, R.L., Mueser, K.T., Wade, J.H., & Sayers, S.L. (1990a). Role play for assessing the social competence of psychiatric patients. Psychological Assessment: A Journal of Consulting and Clinical Psychology, 2(3), 248-255.

Bellack, A.S., Morrison, R.L., Wixted, J.T., & Mueser, K.T. (1990b). An analysis of social competence in schizophrenia. British Journal of Psychiatry, 156, 809-818.

Bellack, A.S., & Mueser, K.T. (1986). A comprehensive treatment program for schizophrenia and chronic mental illness. Community Mental Health Journal, 22(3), 175-189.

Bellack, A.S., Sayers, M., Mueser, K.T., & Bennett, M. (1994). Evaluation of social problem solving in schizophrenia. Journal of Abnormal Psychology, 103(2), 371-378.

Benton, A., & Hamsher, K. (1978). Multiphasic Aphasia Examination Manual. Iowa City: University Of Iowa.

Berman, I., Viegner, B., Merson, A., Allan, E., Pappas, D., & Green, A.I. (1997). Differential relationships between positive and negative symptoms and neuropsychological deficits in schizophrenia. Schizophrenia Research, 25, 1-10.

Berman, K.F., Zec, R.F., & Weinberger, D.R. (1986). Physiologic Dysfunction of Dorsolateral Prefrontal Cortex in Schizophrenia II. Role of Neuroleptic Treatment, Attention, and Mental Effort. Archives of General Psychiatry, 43(2), 126-135.

Berman, K.F., & Weinberger, D.R. (1991). Functional localization in the brain in schizophrenia. In Allan Tasman & Stephen M.Goldfinger (Eds.), Review of Psychiatry. (pp. 24-59). Washington, DC: American Psychiatric Press.

Berning, L.C., Weed, N.C., & Aloia, M.S. (1998). Interrater reliability of the Ruff Figural Fluency Test. Assessment, 5(2), 181-186.

Berns, S., Jaeger, J., & Douglas, E. (1995). Executive deficits predict role functioning in psychiatric outpatients [Abstract]. Journal of the International Neuropsychological Society, 1, 132-132.

Bilder, R.M. (1997). Neurocognitive impairment in schizophrenia and how it affects treatment options [see comments]. Canadian Journal of Psychiatry, 42(3), 255-264.

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Bilder, R.M., Bogerts, B., Ashtari, M., Wu, H., Alvir, J.M., Jody, D., Reiter, G., Bell, L., & Lieberman, J.A. (1995). Anterior hippocampal volume reductions predict frontal lobe dysfunction in first episode schizophrenia. Schizophrenia Research, 17(1), 47-58.

Bilder, R.M., Lipschutz Broch, L., Reiter, G., Geisler, S.H., Mayerhoff, D.I., & Lieberman, J.A. (1992). Intellectual deficits in first-episode schizophrenia: Evidence for progressive deterioration. Schizophrenia Bulletin, 18, 437-448.

Bilder, R.M., Mukherjee, S., Rieder, R.O., & Pandurangi, A.K. (1985). Symptomatic and neuropsychological components of defect states. Schizophrenia Bulletin, 11(3), 409-419.

Bogerts, B., Ashtari, M., Degreef, G., Alvir, J.M.J., Bilder, R.M., & Lieberman, J.A. (1990). Reduced temporal limbic structure volumes on magnetic resonance images in first episode schizophrenia. Psychiatry Research: Neuroimaging, 35, 1-13.

Bogerts, B., & Falkai, P. (1991). Clinical and neurodevelopmental aspects of brain pathology in schizophrenia. In S. A. Mednick, T. D. Cannon, CE. Barr, & J. M. LaFosse (Eds.), Developmental Neuropathology of Schizophrenia. (pp. 93-120).

Bornstein, R.A. (1985). Normative data on selected neuropsychological measures from a nonclinical sample. Journal of Clinical Psychology, 41(5), 651-659.

Bowen, L., Wallace, C.J., Glynn, S.M., Nuechterlein, K.H., Lutzker, J.R., & Kuehnel, T.G. (1994). Schizophrenic individuals' cognitive functioning and performance in interpersonal interactions and skills training procedures. Journal of Psychiatric Research, 28(3), 289-301.

Breier, A., Schreiber, J.L., Dyer, J., & Pickar, D. (1991). National Institute of Mental Health longitudinal study of chronic schizophrenia: Prognosis and predictors of outcome. Archives of General Psychiatry, 48, 239-246.

Breier, A., Schreiber, J.L., Dyer, J., & Pickar, D. (1992). Course of illness and predictors of outcome in chronic schizophrenia: Implications for pathophysiology. British Journal of Psychiatry, 161 (Suppl.18), 38-43.

Brekke, J., Raine, A., Ansel, M., Lencz, T., & Bird, L. (1997). Neuropsychological and psychophysiological correlates of psychosocial functioning in schizophrenia. Schizophrenia Bulletin, 23(1), 19-26.

Brekke, J.S., Raine, A., & Thomson, C. (1995). Cognitive and psychophysiological correlates of positive, negative, and disorganized symptoms in the schizophrenia spectrum. Psychiatry Research, 57(3), 241-250.

Brickenkamp, R. (1981). Concentration-Endurance Test Manual. (5 ed.). Gottingen: Verlag fur Psychologie.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Brown, K.W., & White, T. (1992). Syndromes of chronic schizophrenia and some clinical correlates. British Journal of Psychiatry, 161, 317-322.

Buchanan, R.W., & Carpenter, W.T.J. (1997). The neuroanatomies of schizophrenia. Schizophrenia Bulletin, 23(3), 367-372.

Buchanan, R.W., Strauss, M.E., Kirkpatrick, B., Holstein, C., Breier, A., & Carpenter, W.T., Jr. (1994). Neuropsychological impairments in deficit vs nondeficit forms of schizophrenia. Archives of General Psychiatry, 51(10), 804-811.

Capleton, R.A. (1996). Cognitive function in schizophrenia: Association with negative and positive symptoms. Psychological Reports, 78, 123-128.

Carling, P. (1995). Housing and supports in psychiatric disability. Psychotherapy & Rehabilitation Research Bulletin, 4, 12-16.

Carpenter, W.T., & Strauss, J.S. (1991). The prediction of outcome in schizophrenia: IV. Eleven-year follow-up of the Washington IPSS cohort. Journal of Nervous and Mental Disease, 179(9), 517-525.

Carson, R.C., & Sanislow, C.A. (1993). The schizophrenias. In P. B. Sutker & H. E. Adams (Eds.), Comprehensive Handbook of Psychopathology (2nd ed). (pp. 295-333). New York: Plenum Press.

Cassens, G., Inglis, A.K., Appelbaum, P.S., & Gutheil, T.G. (1990). Neuroleptics: Effects on neuropsychological function in chronic schizophrenic patients. Schizophrenia Bulletin, 16, 477-499.

Cassidy, J.J., Easton, M., Capelli, C., Singer, A., & Bilodeau, A. (1996). Cognitive remediation of persons with severe and persistent mental illness. Psychiatric Quarterly, 67(4), 313-321.

Chapman, L.J., & Chapman, J.P. (1973). Problems in the measurement of cognitive deficit. Psychological Bulletin, 79(6), 380-385.

Chua, S.E., & McKenna, P.J. (1995). Schizophrenia--a brain disease? A critical review of structural and functional cerebral abnormality in the disorder. British Journal of Psychiatry, 166(5), 563-582.

Ciompi, L. (1980). Catamnestic long-term study on the course of life and aging of schizophrenics. Schizophrenia Bulletin, 6(4), 606-618.

Condray, R., van, K.D., Steinhauer, S.R., Kasparek, A., & Yao, J.K. (1995). Language comprehension in schizophrenia: Trait or state indicator? Biological Psychiatry, 38(5), 287-296.

Cooper, J.E. (1972). Psychiatric Diagnosis in New York and London: A Comparative Study of Mental Hospital Admissions. London: Oxford U. Press.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Cornblatt, B.A., & Keilp, J.G. (1994). Impaired attention, genetics, and the pathophysiology of schizophrenia [published erratum appears in Schizophr Bull 1994; 20(2):248]. Schizophrenia Bulletin, 20(1), 31-46.

Cornblatt, B.A., Lenzenweger, M.F., Dworkin, R.H., & Erlenmeyer-Kimling, L. (1985). Positive and negative schizophrenic symptoms, attention, and information processing. Schizophrenia Bulletin, 11, 397-408.

Corrigan, P.W., Green, M.F., & Toomey, R. (1994). Cognitive correlates to social cue perception in schizophrenia. Psychiatry Research, 53(2), 141-151.

Crow, T.J. (1980a). Discussion. British Journal of Psychiatry, 137, 383-386.

Crow, T.J. (1980b). Molecular pathology of schizophrenia. British Medical Journal, 280, 66-68.

Czobor, P., Bitter, I., & Volavka, J. (1991). Relationship between the Brief Psychiatric Rating Scale and the Scale for the Assessment of Negative Symptoms: A study of their correlation and redundancy. Psychiatry Research, 36, 129-139.

Deister, A., & Marneros, A. (1993). Long-term stability of subtypes in schizophrenic disorders: A comparison of four diagnostic systems. European Archives of Psychiatry and Clinical Neuroscience, 242(4), 184-190.

DeLisi, L.E., Sakuma, M., Kushner, M., Finer, D.L., Hoff, A.L., & Crow, T.J. (1997). Anomalous cerebral asymmetry and language processing in schizophrenia. Schizophrenia Bulletin, 23(2), 255-271.

Dickerson, F., Boronow, J.J., Ringel, N., & Parente, F. (1996). Neurocognitive deficits and social functioning in outpatients with schizophrenia. Schizophrenia Research, 21(2), 75-83.

Diller, L. (1987). Neuropsychological rehabilitation. In M. Meier, A. Benton, & L. Diller (Eds.), Neuropsychological Rehabilitation. (pp. 3-18). New York: The Guilford Press.

Endicott, J., & Spitzer, R.L. (1978). A diagnostic interview: The Schedule for Affective Disorders and Schizophrenia. Archives of General Psychiatry, 35, 837-844.

Falkai, P., & Bogerts, B. (1995). Neuropathology of Schizophrenia. In S. R. Hirsch & D. R. Weinberger (Eds.), Schizophrenia. (pp. 275-292). Oxford: Blackwell Science Ltd.

Fein, R. (1958). Economics of Mental Illness. New York: Basic Books.

First, M., Spitzer, R., Gibbon, M., & Williams, J. (1995). Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (SCID-I/P, Version 2.0). Biometric Research Department New York State Psychiatric Institute.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Flashman, L.A., Torres, D.S., O'Leary, D.S., Arndt, S., & Andreasen, N.C. (1995). Neuropsychological deficit in patients with schizophrenia: And effect size strategy. Schizophrenia Research, 15, 117

Flaum, M., Arndt, S., & Andreasen, N.C. (1990). The role of gender in studies of ventricular enlargement in schizophrenia: A predominantly male effect. American Journal of Psychiatry, 147(10), 1327-1332.

Folstein, M.F., Folstein, S.E., & McHugh, P.R. (1975). "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research, 12(3), 189-198.

Frith, C.D. (1992). The Cognitive Neuropsychology of Schizophrenia. East Sussex: Lawrence Erlbaum Associates Ltd.

Gervey, R., & Bedell, J.R. (1994). Supported employment in vocational rehabilitation. In J. R. Bedell (Ed.), Psychological Assessment and Treatment of Persons with Severe Mental Disorders. (pp. 151-175). Washington, D.C.: Taylor and Francis.

Gold, J.M., Carpenter, C., Randolph, C., Goldberg, T.E., & Weinberger, D.R. (1997). Auditory working memory and Wisconsin Card Sorting Test performance in schizophrenia. Archives of General Psychiatry, 54(2), 159-165.

Gold, J.M., & Harvey, P.D. (1993). Cognitive deficits in schizophrenia. Psychiatric Clinics of North America, 16, 295-312.

Gold, J.M., Randolph, C., Carpenter, C.J., Goldberg, T.E., & Weinberger, D.R. (1992). The performance of patients with schizophrenia on the Wechsler Memory Scale-Revised. The Clinical Neuropsychologist, 6(4), 367-373.

Gold, J.M., & Weinberger, D.R. (1995). Cognitive impairments in schizophrenia. Current Opinion in Neurobiology, 5, 225-230.

Gold, J.M., Hermann, B.P., Randolph, C., & Wyler, A.R. (1994). Schizophrenia and temporal lobe epilepsy: A neuropsychological analysis. Archives of General Psychiatry, 51, 265-272.

Goldberg, T.E., Gold, J.M., Torrey, E.F., & Weinberger, D.R. (1995). Lack of sex differences in the neuropsychological performance of patients with schizophrenia. American Journal of Psychiatry, 152 (6), 883-888.

Goldberg, T.E., Greenberg, R.D., Griffin, S.J., Gold, J.M., Kleinman, J.E., Pickar, D., Schulz, S.C., & Weinberger, D.R. (1993). The effect of clozapine on cognition and psychiatric symptoms in patients with schizophrenia [see comments]. British Journal of Psychiatry, 162, 43-48.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Goldberg, T.E., Ragland, J.D., Torrey, E.F., Gold, J.M., Bigelow, L.B., & Weinberger, D.R. (1990). Neuropsychological assessment of monozygotic twins discordant for schizophrenia. Archives of General Psychiatry, 47(11), 1066-1072.

Goldberg, T.E., Torray, E.F., Gold, J.M., Ragland, J.D., Taylor, E., & Weinberger, D.R. (1995). Risk of cognitive impairment in monozygotic twins concordant and discordant for schizophrenia. Schizophrenia Bulletin, 17, 77-84.

Goldberg, T.E., Weinberger, D.R., Berman, K.F., Pliskin, N.H., & Podd, M.H. (1987a). Further evidence for dementia of the prefrontal type in schizophrenia. Archives of General Psychiatry, 44, 1008-1014.

Goldberg, T.E., Weinberger, D.R., Berman, K.F., Pliskin, N.H., & Podd, M.H. (1987b). Further Evidence for dementia of the prefrontal type in schizophrenia? A controlled study of teaching the Wisconsin Card Sorting Test. Archives of General Psychiatry, 44(November), 1008-1014.

Goldberg, T.E., Gold, J.M., & Braff, D.L. (1991). Neuropsychological functioning and time-linked information processing in schizophrenia. In Allan Tasman & Stephen M.Goldfinger (Eds.), Review of Psychiatry. (pp. 60-78). Washington, DC: American Psychiatric Press.

Goldberg, T.E., Torrey, E.F., Gold, J.M., & Ragland, J.D. (1993). Learning and memory in monozygotic twins discordant for schizophrenia. Psychological Medicine, 23, 71-85.

Goldman, R.S., Axelrod, B.N., Tandon, R., Ribeiro, S.C.M., Craig, K., & Berent, S. (1993). Neuropsychological prediction of treatment efficacy and one-year outcome in schizophrenia. Psychopathology, 26, 122-126.

Goldman, R.S., Bilder, R.M., Pappadopulos, E., & Alvir, J.M. (1998). Neuropsychological prediction of functional outcome in first episode schizophrenia. Journal of the International Neuropsychological Society, 4(1), 7-7.

Goldstein, G., Zubin, J., & Pogue G.M.F. (1991). Hospitalization and the cognitive deficits of schizophrenia: The influences of age and education. The Journal of Nervous and Mental Disease, 179(4), 202-206.

Goldstein, J.M. (1996). Sex and brain abnormalities in schizophrenia: Fact or fiction? Harvard Review of Psychiatry, 4 (2), 110-115.

Goldstein, J.M., Seidman, L.J., Goodman, J.M., Koren, D., Lee, H., Weintraub, S., & Tsuang, M.T. (1998). Are there sex differences in neuropsychological functions among patients with schizophrenia? American Journal of Psychiatry, 155(10), 1358-1364.

Goldstein, J.M., Seidman, L.J., Santangelo, S., Knapp, P.H., & Tsuang, M.T. (1994). Are schizophrenic men at higher risk for developmental deficits than schizophrenic

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

women? Implications for adult neuropsychological functions. Journal of Psychiatric Research, 28(6), 483-498.

Good Ellis, M.A., Fine, S.B., Spencer, J.H., & DiVittis, A. (1987). Developing a Role Activity Performance Scale. American Journal of Occupational Therapy, 41, 232-241.

Goodglass, H., & Kaplan, E. (1983). The Assessment of Aphasia and Related Disorders. (2nd ed.). Philadelphia: Lea & Febiger.

Goodman, S.H., Sewell, D.R., Cooley, E.L., & Leavitt, N. (1993). Assessing levels of adaptive functioning: The Role Functioning Scale. Community Mental Health Journal, 29, 119-131.

Gourovitch, M.L., Goldberg, T.E., & Weinberger, D.R. (1997). Verbal fluency deficits in patients with schizophrenia: Semantic fluency is differentially impaired as compared with phonologic fluency. Neuropsychology, 10(4), 573-577.

Grant, D., & Berg, E. (1995). A behavioral analysis of degree of reinforcement and ease of shifting to new responses in a Weigl-type card-sorting problem. Journal of Experimental Psychology, 38, 404-411.

Green, M.F. (1993). Cognitive remediation in schizophrenia: Is it time yet? American Journal of Psychiatry, 150(2), 178-187.

Green, M.F. (1996). What are the functional consequences of neurocognitive deficits in schizophrenia? American Journal of Psychiatry, 153(3), 321-330.

Green, M.F., & Walker, E.F. (1985). Neuropsychological performance and positive and negative symptoms in schizophrenia. Journal of Abnormal Psychology, 94, 460-469.

Green, M.F., & Walker, E.F. (1986). Attentional performance in positive- and negative-symptom schizophrenia. Journal of Nervous and Mental Disease, 174, 208-213.

Green, R.S., & Gracely, E.J. (1987). Selecting a rating scale for evaluating services to the chronically mentally ill. Community Mental Health Journal, 23, 91-102.

Gunderson, J.G., & Mosher, L.R. (1975). The cost of schizophrenia. American Journal of Psychiatry, 132, 901-906.

Gur, R.E., Mozley, D., Resnick, S.M., Shtasel, D., Kohn, M., Zimmerman, R., Herman, G., Atlas, S., Grossman, R., Erwin, R., & Gur, R.C. (1991). Magnetic resonance imaging in schizophrenia: I. Volumetric analysis of brain and cerebrospinal fluid. Archives of General Psychiatry, 48, 407-412.

Guy, W. (1976). ECDEU Assessment Manual for Psychopharmacology. Rockville: NIMH.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Haas, G.L., Sweeney, D.A., Hein, D.A., Goldman, D., & Deck, M. (1991). Gender differences in schizophrenia [Abstract]. Schizophrenia Research, 4, 277-277.

Hafkenscheid, A. (1991). Psychometric evaluation of a standardized and expanded Brief Psychiatric Rating Scale. Acta Psychiatr Scand, 84(3), 294-300.

Hagger, C., Buckley, P., Kenny, J.T., Friedman, L., Ubogy, D., & Meltzer, H.Y. (1993). Improvement in cognitive functions and psychiatric symptoms in treatment-refractory schizophrenic patients receiving clozapine. Biological Psychiatry, 34, 702-712.

Hall, W., Goldstein, G., Andrews, G., Lapsley, H., Bartels, R., & Silove, D. (1985). Estimating the economic costs of schizophrenia. Schizophrenia Bulletin, 11(4), 598-610.

Harding, C.M., Brooks, G.W., Ashikaga, T., Strauss, J.S., & Breier, A. (1987). The Vermont longitudinal study of persons with severe mental illness: II. Long-term outcome of subjects who respectively met DSM-III criteria for schizophrenia. American Journal of Psychiatry, 144(6), 727-735.

Hare, E.H. (1987). Epidemiology of schizophrenia and affective psychoses. British Medical Bulletin, 43(3), 514-530.

Harrow, M., Marengo, J., Pogue-Geile, M.F., & Pawelski, T. (1987). Schizophrenic deficits in intelligence and abstract thinking: Influence of aging and long-term institutionalization. In N. Miller & G. Coles (Eds.), Schizophrenia and Aging. (pp. 133-144). New York: Guilford Press.

Harrow, M., Sands, J.R., Silverstein, M.L., & Goldberg, J.F. (1997). Course and outcome for schizophrenia versus other psychotic patients: A longitudinal study. Schizophrenia Bulletin, 23(2), 287-303.

Heaton, R., Paulsen, J.S., McAdams, L.A., Kuck, J., Zissok, S., Braff, D., Harris, J., & Jeste, D.V. (1994). Neuropsychological deficits in schizophrenics: Relationship to age, chronicity, and dementia. Archives of General Psychiatry, 51, 469-476.

Heaton, R.K. (1981a). The Wisconsin Card Sorting Test Manual. Odessa: Psychological Resources.

Heaton, R.K., & Crowley, T.J. (1981b). Effects of psychiatric disorders and their somatic treatments on neuropsychological test results. In S. B. Filskov & T. J. Boll (Eds.), Handbook of Clinical Neuropsychology. (pp. 481-525). New York: John Wiley.

Heaton, R.K., & Drexler, M. (1987). Clinical neuropsychological findings in schizophrenia and aging. In N. Miller & G. Coles (Eds.), Schizophrenia and Aging. (pp. 145-161). New York: Guilford Press.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Hedlund, J.L., & Vieweg, B.W. (1990). The Brief Psychiatric Rating Scale (BPRS): A comprehensive review. Journal of Operational Psychiatry, 11, 48-65.

Heinrichs, R.W., & Zakzanis, K.K. (1998). Neurocognitive deficit in schizophrenia: A quantitative review of the evidence. Neuropsychology, 12(3), 426-445.

Herrig, E. (1995). First person account: A personal experience. Schizophrenia Bulletin, 21(2), 339-342.

Hoff, A.L., Riordan, H., Odonnell, D., Stritzke, P., Neale, C., Boccio, A., Anand, A.K., & DeLisi, L.E. (1992). Anomalous lateral sulcus asymmetry and cognitive function in first-episode schizophrenia. Schizophrenia Bulletin, 18, 257-268.

Hoff, A.L., Riordan, H., O'Donnell, D.W., & Morris, L. (1992). Neuropsychological functioning of first-episode schizophreniform patients. American Journal of Psychiatry, 149(7), 898-903.

Hoffmann, H., & Kupper, Z. (1997). Relationships between social competence, psychopathology and work performance and their predictive value for vocational rehabilitation of schizophrenic outpatients. Schizophrenia Research, 23(1), 69-79.

Hogarty, G.E., & Flesher, S. (1992). Cognitive remediation in schizophrenia: Proceed... with caution! Schizophrenia Bulletin, 18(1), 51-57.

Hollingshead, A. Four Factor Index of Social Status. (Unpublished Manuscript)

Huber, G., Gross, G., Schüttler, R., & Linz, M. (1980). Longitudinal studies of schizophrenic patients. Schizophrenia Bulletin, 6(4), 592-605.

Hyde, T.M., Casanova, M.F., Kleinman, J.E., & Weinberger, D.R. (1991). Neuroanatomical and neurochemical pathology in schizophrenia. In Allan Tasman & Stephen M.Goldfinger (Eds.), Review of Psychiatry. (pp. 7-23). Washington, DC: American Psychiatric Press.

Jablensky, A. (1997). The 100-year epidemiology of schizophrenia. Schizophrenia Research, 28, 111-125.

Jaeger, J., & Berns, S. (1997). Measurement of Functional Disability in neuropsychiatric populations [Abstract]. Journal of the International Neuropsychological Society, 1, 30-30.

Jaeger, J., & Berns, S. (1999). Neuropsychological management, treatment and rehabilitation of psychiatric patients. In A. Calev (Ed.), Neuropsychological Functions in Psychiatric Disorders. (pp. in press Washington, D.C.: American Psychiatric Press.

Jaeger, J., & Douglas, E. (1992). Neuropsychiatric rehabilitation for persistent mental illness. Psychiatric Quarterly, 63(1), 71-94.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Jones, E.G., & Akbarian, S. (1995). Potential mechanisms of defective brain development in schizophrenia. In S. A. Mednick & J. M. Hollister (Eds.), Neural Development and Schizophrenia: Theory and Research. (pp. 13-56).

Jones, P., Rodgers, B., Murray, R., & Marmot, M. (1994). Child development risk factors for adult schizophrenia in the British 1946 birth cohort. Lancet, 344, 1398-1402.

Kay, S.R., Fiszbein, S., & Opler, L.A. (1987a). The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophrenia Bulletin, 13(2), 261-276.

Kay, S.R., & Lindenmayer, J.P. (1987b). Outcome predictors in acute schizophrenia. Prospective significance of background and clinical dimensions. Journal of Nervous and Mental Disease, 175, 152-160.

Kendler, K.S., & Diehl, S.R. (1993). The genetics of schizophrenia: A current, genetic-epidemiologic perspective. Schizophrenia Bulletin, 19(2), 261-285.

Kern, R.S., Green, M.F., & Satz, P. (1992). Neuropsychological predictors of skills training for chronic psychiatric patients. Psychiatry Research, 43, 223-230.

King, D.J. (1994). Psychomotor impairment and cognitive disturbances induced by neuroleptics. Acta Psychiatrica Scandinavica Supplementum, 380, 53-58.

Kraepelin, E., & translated by R.M.Barclay. (1919). Dementia Praecox and Paraphrenia. Edinburgh: E. and S. Livingstone.

Lane, E.A., & Albee, G.W. (1964). Early childhood intellectual differences between schizophrenic adults and their siblings. Journal of Abnormal and Social Psychology, 68(2), 193-195.

Langfeldt, G. (1956). The prognosis in schizophrenia. Acta Psychiatrica et Neurologica Scandinavica,. 110 (Suppl), 5-66.

Lawrie, S.M., & Abukmeil, S.S. (1998). Brain abnormality in schizophrenia. British Journal of Psychiatry, 172, 110-120.

Lehman, A., Carpenter, W., Goldman, H., & Steinwachs, D. (1995). Treatment outcomes in schizophrenia: Implications for practice, policy and research. Schizophrenia Bulletin, 21(4), 669-675.

Leonhard, K. (1980). Contradictory issues in the origin of schizophrenia. British Journal of Psychiatry, 136, 437-444.

Levin, S., Yurgelun Todd, D., & Craft, S. (1989). Contributions of clinical neuropsychology to the study of schizophrenia. Journal of Abnormal Psychology, 98(4), 341-356.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Lewine, R.R., Walker, E.F., Shurett, R., Caudle, J., & Haden, C. (1996). Sex differences in neuropsychological functioning among schizophrenic patients. American Journal of Psychiatry, 153(9), 1178-1184.

Lezak, M. (1995). Neuropsychological Assessment. (3 ed.). New York: Oxford University Press.

Lezak, M.D. (1983). Neuropsychological Assessment. (2 ed.). New York: Oxford University Press.

Liberman, R.P. (1997). Neurocognitive deficits in schizophrenia [letter]. American Journal of Psychiatry, 154(3), 443-444.

Liberman, R.P., Mueser, K.T., Wallace, C.J., Jacobs, H.E., Eckman, T., & Massel, H.K. (1986). Training skills in the psychiatrically disabled: Learning coping and competence. Schizophrenia Bulletin, 12(4), 631-647.

Liddle, P.F. (1987). Schizophrenic syndromes, cognitive performance, and neurological dysfunction. Psychological Medicine, 17, 49-57.

Liddle, P.F., Friston, K.J., Frith, C.D., Hirsch, S.R., Jones, T., & Frackowiak, R.S.J. (1992). Patterns of cerebral blood flow in schizophrenia. British Journal of Psychiatry, 160, 179-186.

Lieberman, J.A., Alvir, J.M.J., Woerner, M., Degreef, G., Bilder, R.M., Ashtari, M., Bogerts, B., Mayerhoff, D.I., Geisler, S.H., Loebel, A.D., Levy, D.L., Hinrichsen, G., Szymanski, S., Chakos, M.H., Koreen, A., Borenstein, M., & Kane, J.M. (1992). Prospective study of psychobiology in first-episode schizophrenia at Hillside Hospital. Schizophrenia Bulletin, 18(3), 351-371.

Lysaker, P., Bell, M., & Beam Goulet, J. (1995). Wisconsin Card Sorting Test and work performance in schizophrenia. Psychiatry Research, 56(1), 45-51.

MacDonald-Wilson, K.L., Revell, G.W., Hguyen, N.H., & Peterson, M.E. (1991). Supported employment outcomes for people with psychiatric disability: A comparative analysis. Journal Of Vocational Rehabilitation, 1(3), 30-44.

Malla, A.K., Lazosky, A., McLean, T., Rickwood, A., Cheng, S., & Norman, R.M. (1997). Neuropsychological assessment as an aid to psychosocial rehabilitation in severe mental disorders. Psychiatric Rehabilitation Journal, 21(2), 169-173.

Manschreck, T.C. (1983). Psychopathology of motor behavior in schizophrenia. Progress in Experimental Personality Research, 12, 53-94.

Marengo, J. (1994). Classifying the courses of schizophrenia. Schizophrenia Bulletin, 20(3), 519-536.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Marneros, A., Rohde, A., & Deister, A. (1995). Validity of the negative/positive dichotomy of schizophrenic disorders under long-term conditions. Psychopathology, 28(1), 32-37.

Massel, K.H., Corrigan, P.W., Liberman, R.P., & Milan, M.A. (1991). Conversation skills training of thought-disordered schizophrenic patients though attention focusing. Psychiatry Research, 38, 51-61.

Matthews, C.G., & Love, H. (1964). Instructions Manual for the Adult Neuropsychology Test Battery. Madison, WI: University of Wisconsin Medical School.

McFie, J. (1975). Assessment of Organic Intellectual Impairment. New York: Academic Press.

McGlashan, T.H. (1986). The prediction of outcome in chronic schizophrenia IV: The chestnut lodge follow-up study. Archives of General Psychiatry, 43, 167-176.

McGlashan, T.H., Carpenter, W.T., & Bartko, J.J. (1988). Issues of design and methodology in long-term followup studies. Schizophrenia Bulletin, 14, 569-574.

Medalia, A., Gold, J.M., & Merriam, A.E. (1988). The effects of neuroleptics on neuropsychological test results of schizophrenics. Archives of Clinical Neuropsychology, 3, 249-271.

Meltzer, H.Y. (1992). Dimensions of outcome with clozapine. British Journal of Psychiatry, 17, 46-53.

Meltzer, H.Y., Thompson, P.A., Lee, M.A., & Ranjan, R. (1996). Neuropsychologic deficits in schizophrenia: Relation to social function and effect of antipsychotic drug treatment. Neuropsychopharmacology, 14(3 Suppl), 27S-33S.

Moller, H., Schmid B.W., Cording T.C., Wittchen, H.U., & et al. (1988). Psychopathological and social outcome in schizophrenia versus affective/schizoaffective psychoses and prediction of poor outcome in schizophrenia: Results from a 5-8 year follow-up. Acta-Psychiatrica-Scandinavia, 77(4), 379-389.

Morlan, K.K., & Tan, S. (1998). Comparison of the Brief Psychiatric Rating Scale and the Brief Symptom Inventory. Journal of Clinical Psychology, 54(7), 885-894.

Morrison, R.L., Bellack, A.S., Wixted, J.T., & Mueser, K.T. (1990). Positive and negative symptoms in schizophrenia: A cluster-analytic approach. Journal of Nervous and Mental Disease, 178(6), 377-384.

Mueser, K.T., Bellack, A.S., Douglas, M.S., & Morrison, R.L. (1991a). Prevalence and stability of social skill deficits in schizophrenia. Schizophrenia Research, 5, 167-176.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Mueser, K.T., Bellack, A.S., Douglas, M.S., & Wade, J.H. (1991b). Prediction of social skill acquisition in schizophrenic and major affective disorder patients from memory and symptomatology. Psychiatry Research, 37, 281-296.

Mueser, K.T., Bellack, A.S., Morrison, R.L., & Wixted, J.T. (1990). Social competence in schizophrenia: Premorbid adjustment, social skill and domains of functioning. Journal of Psychiatric Research, 24(1), 51-63.

Munroe-Blum, H., Collins, E., Nuttall, S., & McCleary, L. The Social Dysfunction Index (SDI) for patients with schizophrenia and related disorders. (un published manuscript)

Murray, C.J.L., & Lopez, A.D. (1996). The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability from Diseases, Injuries, and Risk Factors in 1990 and projected to 2020. Cambridge: Harvard University Press.

Nopoulos, P., Flashman, L., Flaum, M., & Arndt, S. (1994). Stability of cognitive functioning early in the course of schizophrenia. Schizophrenia Research, 14(1), 29-37.

Nuechterlein, K.H., Edell, W.S., Norris, M., & Dawson, M.E. (1986). Attentional vulnerability indicators, thought disorder, and negative symptoms. Schizophrenia Bulletin, 12(3), 408-426.

Oldfield, R.C. (1971). The assessment and analysis of handedness: The Edinburgh Inventory. Neuropsychologia., 9(1), 97-113.

Overall, J.E., & Gorham, D.R. (1988). The Brief Psychiatric Rating Scale (BPRS): Recent developments in ascertainment and scaling. Psychopharmacology Bulletin, 24(1), 97-98.

Overall, J.E., Hollister, L.E., & Pichot, P. (1967). Major psychiatric disorders: A four-dimensional model. Archives of General Psychiatry, 16(2), 146-151.

Paulsen, J.S., Heaton, R.K., Sadek, J.R., Perry, W., Delis, D.C., Braff, D.L., Kuck, J., Zisook, S., & Jeste, D.V. (1995). The nature of learning and memory impairments in schizophrenia. Journal of the International Neuropsychological Society, 1, 88-99.

Pearlson, G.D., Garbacz, D.J., Breakey, W.R., Ahn, H.S., & DePaulo, J.R. (1984). Lateral ventricular enlargement asociated with persistent unemployment and negative symptoms in both schizophrenia and bipolar disorder. Psychiatry Research, 12, 1-9.

Penn, D.L. (1991). Cognitive rehabilitation of social deficits in schizophrenia: A direction of promise or following a primrose path. Psychosocial Rehabilitation Journal, 15(1), 27-41.

Penn, D.L., Mueser, K.T., Spaulding, W., Hope, D.A., & Reed, D. (1995). Information processing and social competence in chronic schizophrenia. Schizophrenia Bulletin, 21(2), 269-281.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Perlick, D., Mattis, S., Stastny, P., & Silverstein, B. (1992a). Negative symptoms are related to both frontal and nonfrontal neuropsychological measures in chronic schizophrenia. Archives of General Psychiatry, 49(3), 245-246.

Perlick, D., Mattis, S., Stastny, P., & Teresi, J. (1992b). Neuropsychological discriminators of long-term inpatient or outpatient status in chronic schizophrenia. Journal of Neuropsychiatry and Clinical Neuroscience, 4(4), 428-434.

Perlick, D., Stastny, P., Mattis, S., & Teresi, J. (1992c). Contribution of family, cognitive and clinical dimensions to long-term outcome in schizophrenia. Schizophrenia Research, 6, 257-265.

Randolph, C., Goldberg, T.E., & Weinberger, D.R. (1998). Clinical Neuropsychology. (Third ed.). New York: Oxford University Press.

Reitan, R., & Davidson, L. (1974). Clinical Neuropsychology: Current Status and Applications. New York: Hemisphere.

Rosenthal, D. (1970). Genetic Theory and Abnormal Behavior. New York: McGraw-Hill Inc.

Ruff, R.M., Light, R.H., & Evans, R.W. (1987). The Ruff Figural Fluency Test: A normative study with adults. Developmental Neuropsychology, 3(1), 37-51.

Rupp, A., & Keith, S.J. (1993). The costs of schizophrenia: Assessing the burden. Psychiatric Clinics of North America, 16(2), 413-423.

Saykin, A.J., Gur, R.C., Gur, R.E., Mozley, D., Mozley, L., Resnick, S.M., Kester, B., & Stafiniak, P. (1991). Neuropsychological function in schizophrenia: Selective impairment in memory and learning. Archives of General Psychiatry, 48, 618-624.

Saykin, A.J., Shtasel, D.L., Gur, R.E., Kester, D.B., Mozley, L.H., Stafiniak, P., & Gur, R.C. (1994). Neuropsychological deficits in neuroleptic naive patients with first-episode schizophrenia. Archives of General Psychiatry, 51, 124-131.

Schooler, N.R. (1993). Antipsychotic medications and schizophrenia: Effects in acute and maintenance treatment of the illness. In R. L. Cromwell & S. H. Snyder (Eds.), Schizophrenia: Origins, Process, Treatment, and Outcome. (pp. 284-295). New York: Oxford University Press.

Schooler, N.R., Hogarty, G.E., & Weissman, M.M. (1979). Social Adjustment Scale II (SAS II). In W. A. Hargreaves, C. C. Attkisson, & J. E. Sorenson (Eds.), Resource materials for community mental health evaluators, publication No. (ADM) 79-328. (pp. 290-330). Washington, D.C.: U.S. Dept. of Health, Education and Welfare.

Schooler, N.R., Keith, S.J., Severe, J.B., & Matthews, S. (1989). Acute treatment response and short term outcome in schizophrenia: First results of the NIMH treatment

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

strategies in schizophrenia study. Treatment strategies in schizophrenia collaborative study group. Psychopharmacology Bulletin, 25(3), 331-335.

Schulz, S.C. (1991). Genetics of schizophrenia: A status report. In Allan Tasman & Stephen M.Goldfinger (Eds.), Review of Psychiatry. (pp. 79-97). Washington, DC: American Psychiatric Press.

Seidman, L.J., Goldstein, J.M., Goodman, J.M., Koren, D., Turner, W.M., Faraone, S.V., & Tsuang, M.T. (1997). Sex differences in olfactory identification and Wisconsin Card Sorting performance in schizophrenia: Relationship to attention and verbal ability. Biological Psychiatry, 42(2), 104-115.

Seidman, L.J., Pepple, J.R., Faraone, S.V., Kremen, W.S., & et al. (1993). Neuropsychological performance in chronic schizophrenia in response to neuroleptic dose reduction. Biological Psychiatry, 33, 575-584.

Silverstein, M.L., Fogg, L., & Harrow, M. (1991). Prognostic significance of cerebral status: Dimensions of clinical outcome. Journal of Nervous and Mental Disease, 179(9), 534-539.

Smet, I.C., Goldman, R.S., Bartok, J., Decker, L., Tandon, R., & Berent, S. (1995). Stability of neuropsychological functioning across an acute episode [Abstract]. Journal of the International Neuropsychological Society, 1, 132-132.

Spaulding, W.D. (1992). Design prerequisites for research on cognitive therapy for schizophrenia. Schizophrenia Bulletin, 18(1), 39-42.

Spitzer, R.L., Endicott, J., & Robins, E. (1978). Research diagnostic criteria: Rationale and reliability. Archives of General Psychiatry, 35, 773-782.

Spitzer, R.L., Gibbon, M., & Endicott, J. (1975). The Global Assessment Scale (GAS). New York: New York State Psychiatric Institute.

Spohn, H.E., & Strauss, M.E. (1989). Relation of neuroleptic and anticholinergic medication to cognitive functions in schizophrenia. Journal of Abnormal Psychology, 98(4), 367-380.

Spreen, O., & Strauss, E. (1998). A Compendium of Neuropsychological Tests. (Second ed.). New York: Oxford University Press.

Spring, B., & Ravdin, L. (1992). Cognitive remediation in schizophrenia: Should we attempt it? Schizophrenia Bulletin, 18(1), 15-20.

Stein, L.I., & Test, M.A. (1980). Alternative to mental hospital treatment: I. Conceptual model, treatment program, and clinical evaluation. Archives of General Psychiatry, 37(4), 392-397.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Stern, R.G., Kahn, R.S., & Davidson, M. (1993). Predictors of response to neuroleptic treatment in schizophrenia. Psychiatric Clinics of North America, 16, 313-338.

Strauss, J.S., & Carpenter, W.T. (1972). The prediction of outcome in schizophrenia: I. Characteristics of outcome. Archives of General Psychiatry, 27, 739-746.

Strauss, J.S., & Carpenter, W.T. (1974). The prediction of outcome in schizophrenia. II. Relationships between predictors and outcome variables: A report from the WHO International Pilot Study of Schizophrenia. Archives of General Psychiatry, 31, 37-42.

Strauss, J.S., & Carpenter, W.T. (1978). The prognosis of schizophrenia: Rationale for a multidimensional concept. Schizophrenia Bulletin, 4, 56-67.

Strauss, J.S., Carpenter, W.T., & Bartko, J.J. (1974). The diagnosis and understanding of schizophrenia: III. Speculations on the processes that underlie schizophrenic symptoms and signs. Schizophrenia Bulletin, 1(11), 61-69.

Strauss, J.S., & Carpenter, W.T.J. (1977). Prediction of outcome in schizophrenia: III. Five-year outcome and its predictors. Archives of General Psychiatry, 34, 159-163.

Stuve, P., Erickson, R.C., & Spaulding, W.D. (1991). Cognitive Rehabilitation: The next step in psychiatric rehabilitation. Psychosocial Rehabilitation Journal, 15(1), 9-26.

Suddath, R.L., Christison, G.W., Torrey, E.F., Casanova, M.F., & Weinberger, D.R. (1990). Anatomical abnormalities in the brains of monozygotic twins discordant for schizophrenia. New England Journal of Medicine, 322(12), 789-794.

Sweeney, J.A., Haas, G.L., Keilp, J.G., & Long, M. (1991). Evaluation of the stability of neuropsychological functioning after acute episodes of schizophrenia: One-year followup study. Psychiatry Research, 38, 63-76.

Syvalahti, E.K. (1994). Biological factors in schizophrenia: Structural and functional aspects. British Journal of Psychiatry, Suppl(23), 9-14.

Szymanski, S., Kane, J.M., & Lieberman, J.A. (1991). A selective review of biological markers in schizophrenia. Schizophrenia Bulletin, 17(1), 99-111.

Tamminga, C. (1997). Neuropsychiatric aspects of schizophrenia. In S. Yudofsky & R. Hales (Eds.), The American Psychiatric Press Textbook of Neuropsychiatry. (pp. 855-882). Washington, D.C, American Psychiatric Press, Inc.

Tamminga, C.A., Thaker, G.K., Buchanan, R., Kirkpatrick, B., Alphs, L.D., Chase, T.N., & Carpenter, W.T. (1992). Limbic system abnormalities identified in schizophrenia using positron emission tomography with fluorodeoxyglucose and neocortical alterations with deficit syndrome. Archives of General Psychiatry, 49(7), 522-530.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Thomas, P., Kearney, G., Napier, E., Ellis, E., Leudar, I., & Johnston, M. (1995). Speech and language in first onset psychosis differences between people with schizophrenia, mania, and controls. British Journal of Psychiatry, 168(3), 337-343.

Torrey, W., Becker, D., & Drake, R. (1995). Rehabilitation day treatment vs supported employment: II. Consumer, family and staff reactions to a program change. Psychosocial Rehabilitation Journal, January(3), 67-75.

Townes, B.D., Martin, D.C., Nelson, D., Prosser, R., Pepping, M., Maxwell, J., Peel, J., & Preston, M. (1985). Neurobehavioral approach to classification of psychiatric patients using a competency model. Journal of Consulting and Clinical Psychology, 53, 33-42.

Trotter, S., Minkoff, K., Harrison, K., & Hoops, J. (1988). Supported work: An innovative approach to the vocational rehabilitation of persons who are psychiatrically disabled. Rehabilitation Psychology, 33(1), 27-37.

Tsuang, M.T., & Winokur, G. (1974). Criteria for subtyping schizophrenia. Clinical differentiation of hebephrenic and paranoid schizophrenia. Archives of General Psychiatry, 31, 43-47.

Van Os, J., Fahy, T.A., Jones, P., Harvey, I., Lewis, S., Williams, M., Toone, B., & Murray, R. (1995). Increased intracerebral cerebrospinal fluid spaces predict unemployment and negative symptoms in psychotic illness: A prospective study. British Journal of Psychiatry, 166(6), 750-758.

Velligan, D.I., Mahurin, R.K., Diamond, P.L., Hazleton, B.C., Eckert, S.L., & Miller, A.L. (1997). The functional significance of symptomatology and cognitive function in schizophrenia. Schizophrenia Research, 25, 21-31.

Ventura, J., Liberman, R.P., Green, M.F., Shaner, A., & Mintz, J. (1998). Training and quality assurance with the Structured Clinical Interview for DSM-IV (SCID-I/P) [In Process Citation]. Psychiatry Research, 79(2), 163-173.

Volavka, J., Cooper, T.B., Czobor, P., & Meisner, M. (1995). Plasma haloperidol levels and clinical effects in schizophrenia and schizoaffective disorder. Archives of General Psychiatry, 52(10), 837-845.

Walker, E.F., & Green, M.F. (1982). Soft signs of neurological dysfunction in schizophrenia: An investigation of lateral performance. Biological Psychiatry, 17(3), 381-386.

Walker, E.F., Savoie, T., & Davis, D. (1994). Neuromotor precursors of schizophrenia. Schizophrenia Bulletin, 20(3), 441-451.

Wallace, C.J. (1986). Functional assessment in rehabilitation. Schizophrenia Bulletin, 12, 604-630.

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Wechsler, D. (1981). Wechsler Adult Intelligence Scale - Revised. San Antonio: The Psychological Corporation - Harcourt Brace Jovanovich, Inc.

Wechsler, D. (1987). Wechsler Memory Scale - Revised. New York: Psychological Corporation.

Weinberger, D.R., & Berman, K.F. (1988). Neuropathological studies of schizophrenia: A selective review. Schizophrenia Bulletin, 9, 193-212.

Weinberger, D.R., Berman, K.F., & Zec, R.F. (1986). Physiologic dysfunction of dorsolateral prefrontal cortext in schizophrenia: I. Regional cerebral blood flow evidence (rCBF). Archives of General Psychiatry, 43, 114-125.

Weinberger, D.R., & Gallhofer, B. (1997). Cognitive function in schizophrenia. International Clinical Psychopharmacology, 12(4), S29-S36

Weissman, M.M. (1975). The assessment of social adjustment. Archives of General Psychiatry, 32, 357-364.

Weissman, M.W., Sholomskas, D., & John, K. (1981). The assessment of social adjustment: An update. Archives of General Psychiatry, 38, 1250-1258.

Wing, J.K. (1995). Concepts of schizophrenia. In S. R. Hirsch & D. R. Weinberger (Eds.), Schizophrenia. (pp. 3-14). Oxford: Blackwell Science Ltd.

Woerner, M.G., Mannuzza, S., & Kane, J.M. (1988). Anchoring the BPRS: An aid to improved reliability. Psychopharmacology Bulletin, 24(1), 112-121.

Wyatt, R.J., Henter, I., Leary, M.C., & Taylor, E. (1995). An economic evaluation of schizophrenia--1991. Social Psychiatry and Psychiatric Epidemiology, 30(5), 196-205.

Wykes, T., & Dunn, G. (1992). Cognitive deficit and the prediction of rehabilitation success in a chronic psychiatric group. Psychological Medicine, 22, 389-398.

Wykes, T., Sturt, E., & Katz, R. (1990). The prediction of rehabilitative success after three years: The use of social, symptom and cognitive variables. British Journal of Psychiatry, 157, 865-870.

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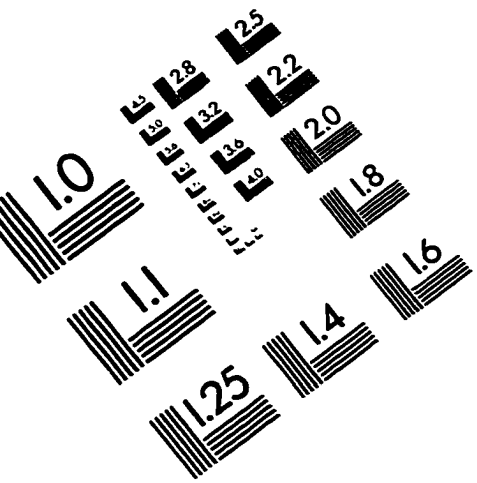
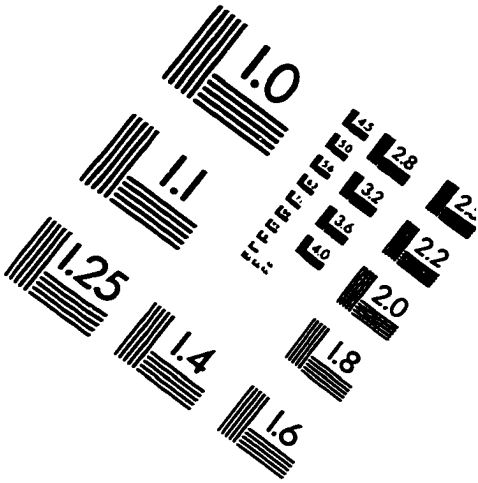
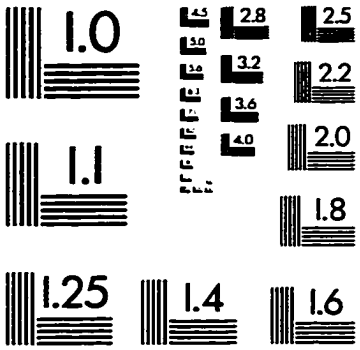
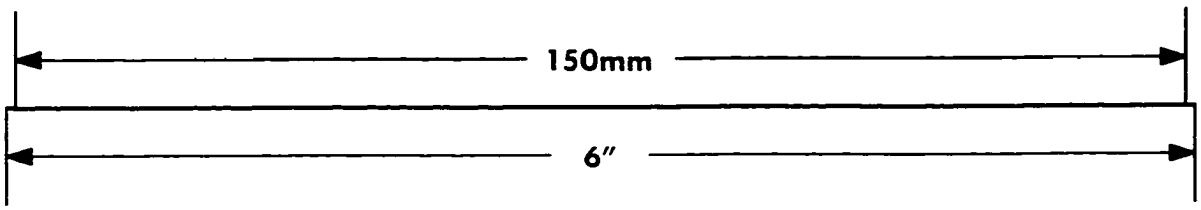
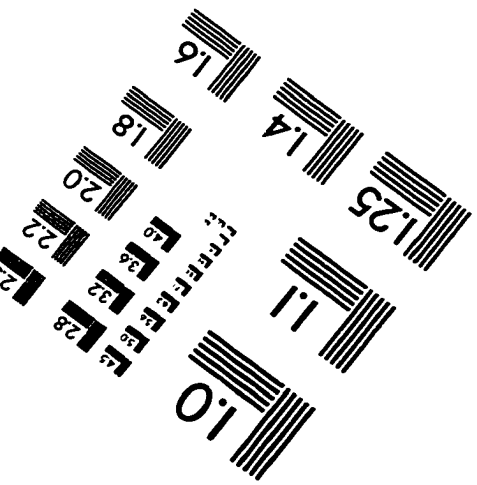
IMAGE EVALUATION
TEST TARGET (QA-3)

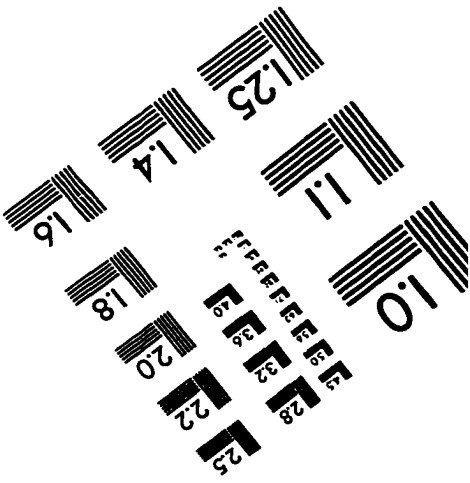












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