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Phenomenological and neuropsychological correlates of positive and negative dimensions in schizophrenia

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Phenomenological and Neuropsychological Correlates of Positive and Negative Dimensions in Schizophrenia

by

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Abstract

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of Positive and Negative Dimensions
in Schizophrenia
by
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While productive features of schizophrenia have become accepted as pathognomonic of the disorder, investigators have proposed that schizophrenics may be phenomenologically subtyped into positive and negative syndromes. Positive syndrome schizophrenics are those whom display a predominance of productive symptoms while patients in the negative syndrome group tend to demonstrate defect symptoms. The latter group is also marked by a degeneration of brain and behavior. In comparison to the positive group, negative syndrome patients are thought to display: (1) a greater degree of neuropsychological dysfunction, particularly that related to anterior functioning; (2) cognitive developmental impairment; (3) defects of affect related to withdrawal; (4) demographic and historical differences such that the negative syndrome is associated with an earlier age of onset, less education, a greater duration of illness, longer hospitalization, and a greater degree of motor abnormalities.

The association of these characteristics to positive and negative phenomenological presentation was studied in a sample of 35 schizophrenic inpatients on the research unit of a medical school affiliated psychiatric center. Correlations within and between predefined sets of positive and negative symptoms failed to support the hypothetical homogeneity of positive and negative syndromes. It was found, however, that the negative syndrome appears to be the more homogeneous of the two. Although clusters of "core" negative and positive symptoms were identified in a Principal Components Analysis, another cluster involving overlap between positive and negative symptoms was also found.

Neither positive nor negative syndromes were related to cognitive developmental or to subject characteristics (demographic, historical, and treatment) in ways that were hypothesized when data were analyzed from a dichotomous perspective, that is, positive or negative group membership. They did, however, differ in their performance on a neuropsychological variable associated with anterior dysfunction.

Despite the paucity of significant findings during dichotomous analyses, dimensional (degree of positivity vs. negativity) analyses uncovered relationships consistent with several hypotheses. Specifically, (1) the hypothesized greater degree of anterior dysfunction in patients displaying a predominance of negative symptoms was partially supported. In addition, a "core"

negative symptoms factor was related to both left anterior and left hemisphere impairment; (2) a greater degree of negativity was significantly related to longer hospitalization and higher neuroleptic dose; and (3) greater degree of negativity was also associated with a greater degree of emotional unrelatedness and expressive immobility.

Degree of positivity, on the other hand, was found to be related to an earlier age of onset and inappropriateness of affect. Neuropsychologically, the positive patients performed in a manner consistent with motor-related anterior dysfunction and bilateral cerebral dysfunction.

Several hypotheses were not supported by the data. Specifically, significant relationships were not found between the negative syndrome and demographic, historical, or cognitive developmental variables. Possible reasons for this lack of support are discussed.

Finally, issues related to sample selection are discussed as they are important to the interpretation of these findings and their relationship to those of other investigators. In addition, suggestions for future research are discussed within the context of this study's findings.

This work is dedicated to my parents

Paul Sr. and Fredesuinda

without whose encouragement and

support it would never

have been undertaken

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Well it's finally time to lay back and put up my feet, that is, until tommorrow.

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Statement Of The Problem

Given the complex interactive factors which contribute to etiological and phenomenological aspects of the schizophrenic process, the positive/negative approach to subtyping has become popular based on both its heuristic value and the fact that it includes a number of different approaches ranging from phenomenology to pathophysiology under the rubric of a comprehensive subtyping hypothesis. Such an approach directly addresses the objection raised by Jeste, et al. (1982) and by Kety (1980) that schizophrenia has become nothing more than an umbrella classification for a variety of disorders. Their recommendation, which represents a more recent development in the evolution of thought concerning this disorder, is that subtyping of schizophrenia should not be unitarily based on phenomenology but, rather, should include multiple behavioral and biological dimensions as well.

In the past, neuropsychological assessments were frequently used in the differential diagnosis of schizophrenia from brain damage (organicity). However, such a differential diagnosis is inappropriate today given what we know about structural and metabolic abnormalities which are often a part of this disorder. Specifically, one can expect schizophrenics to present with varying degrees of 'organicity.' Thus, more recent approaches to subtyping the schizophrenic disease have employed multifactorial techniques based on phenomenology, neuropsychological functioning, presence or absence of CT Scan abnormalities, etc. The utilization of such an approach will likely lead to the distinguishing of subgroups based upon clear differences in presentation.

The positive/negative nosological classification of schizophrenia has proven itself to be of significant heuristic value given its relatively recent popularity (Andreasen, 1982; Crow, 1980a). However, the validity of these subgroups is an even more recent phenomenon (Opler, Fiszbein, & Kay, 1986; Walker, 1987). Few studies have examined the positive/negative dimension from a "multidisciplinary" perspective.

Most studies thus far have concentrated on the phenomenology of the positive vs. negative schizophrenic with few adding neuropsychological tests to their protocol. Very often the neuropsychological assessment in these studies has been composed of only two or three tests without a well thought out conceptual basis for their inclusion. Furthermore, the few neuropsychological studies of this nosological classification and the fewer multifactorial studies employing phenomenological, neuroimaging, and neuropsychological techniques have attempted to derive subgroups without the use of a well validated instrument which could separate out the positive from the negative schizophrenics. Many of these studies were limited to symptom "checklists" in teasing out positive from negative phenomenology rather than a standardized rating scale which would provide clearcut descriptions of individual sypmptoms as well as anchoring points for the assessment of the severity of each symptom. Whether or not a symptom was present was usually left to the intuitive skill of the rater with relatively little guidance being provided from the literature. What guidance was provided (Andreasen, 1983, 1984; Lewine, Fogg, & Meltzer, 1983) was usually not well validated. This, of course, leaves open the question as to whether or not those patients thought to be positive or negative were actually so. In fact, many of these studies examined positive and negative subtypes from a dichotomous perspective exclusively and, of course, recent findings suggest that positive and negative phenomenology should be conceptualized dimensionally as well (Kay & Opler, 1987a). These data clearly demonstrate that most schizophrenic patients present with both positive and negative symptoms. However, they can reliably be separated into those who present with predominantly positive or predominantly negative phenomenlogies (Kay, Fiszbein, & Opler, 1987; Opler, Fiszbein & Kay, 1987). It has only been very recently that a well validated instrument for the assessment of positive and negative symptoms has become available (Kay, Fiszbein, & Opler, 1987; Kay, Opler, & Lindenmayer 1988). The development of this instrument has made it possible to reliably assign schizophrenic subjects into predominantly positive or predominantly negative subgroups as well as allowing for a dimensional analysis of relative positivity versus negativity within each subject.

The aims of the proposed study are (1) to investigate the pattern of relationships among clinical ratings and neuropsychological indices of deterioration which have been proposed to differentiate patients with a predominantly positive phenomenological presentation from those exhibiting predominantly negative symptoms (dichotomous analysis); (2) to investigate the same pattern of relationships based on the relative preponderance of positive and negative symptoms within each subject (dimensional anaylsis); (3) to explore potential relationships between phenomenological ratings and functionally specified neuropsychological deficits from the perspective of cognitive domains; and (4) to determine whether predominantly negative subtype schizophrenics demonstrate incomplete cognitive development as has been proposed (Kay & Opler, 1987b).

Introduction

Schizophrenia reigns amongst the major health care problems in the United States with schizophrenics occupying more than half the beds in U.S. psychiatric hospitals (President's Commission on Mental Health, 1978). Approximately one out of every one hundred Americans either has or will experience a schizophrenic episode (Yolles & Kramer, 1969). In addition, the recidivisim rates for the first time schizophrenic discharges has been estimated at approximately fifty percent within two years (Brown, 1960). Given the pervasiveness and presumed heterogeneity of this disorder, recent research on schizophrenia has concentrated on attempting to identify distinct subtypes which might be relevant to etiological, treatment, and prognostic considerations.

To date, the most commonly used approach in subtyping schizophrenia has been the phenomenological method. The schizophrenic disease is not a recent phenomenon, Hippocrates having described a paranoid disorder thousands of years ago. However, it has only been considered as a distinct disorder since Emil Kraepelin first popularized the term Dementia Praecox (Kraepelin, 1896, 1919). He based his classification on causes of the disease, how much of the brain and nervous system it involved, the variety and course of symptoms, as well as on prognosis. While Kraepelin did popularize the term, _dementia praecox_ had already been used by Morel (1860). Morel used the term to describe the intellectual deterioration in one of his patients whose symptoms had begun at the age of fourteen. However, he did not identify a specific cluster of related clinical features which would have permitted the diagnosis of the condition without waiting for ultimate deterioration. Pick, on the other hand, described a subgroup of patients who underwent what he termed "simple deterioration" of cognition while exhibiting few, if any, of the florid hallucinations and delusions characteristic of other patients. Kraepelin was, however, the first to exhaustively describe the phenomenological aspects of this disorder and was one of the first to differentiate dementia praecox from other disorders. He was also the first to divide the schizophrenic patients he observed into three subtypes: the hebephenic, the catatonic, and the paranoid. Later, he came to accept a fourth type, the simple, which was proposed by Bleuler (1911,1950).

Kraepelin believed that mental diseases caused mainly by external conditions were curable, while those caused by constitutional factors were incurable because their source was brain disease or a metabolic disorder. This is pertinent in light of CT Scan data supportive of a neurostructrual influence in a subgroup of schizophrenics who are poor responders to pharmacological treatment and fall within a poorer prognostic category (Goldberg, 1985). Kraepelin believed that dementia praecox was caused by constitutional factors and was thus incurable. Under the heading of dementia praecox, he included the following symptoms: delusions, hallucinations, attentional deficits, and bizarre behavior. Today, most of these symptoms are felt to be pathognomonic of the positive or Type I schizophrenic subtype and there is evidence that these individuals are neuropathologically, neuropsychologically, and prognostically different from the negative or Type II schizophrenic (Andreasen, 1985; Cornblatt et al., 1985; Pogue-Geile & Harrow, 1985). Furthermore, Bleuler wrote that schizophrenia did not represent a singular disease entity:

> ...For the sake of convenience, I use the word [schizophrenia] in the singular although it is apparent that the group includes several diseases ([1911], 1950, p. 8).

Thus, Bleuler may be thought of as being responsible for laying the foundation of a subtyping approach to schizophrenia. Bleuler was also in agreement with Krapelin as to the basic organic foundation of the schizophrenic illness. While agreeing with the widely held belief of his day that mental (psychogenic) causes might produce symptoms or the content of symptoms, he felt that the actual disease itself was organic in origin (Bleuler, 1911, 1950).

Since Bleuler's time, the history of research in schizophrenia has been replete with efforts to subtype this disorder on a phenomenological basis in the hope that it would provide information germane to etiological, treatment, and prognostic considerations. Phenomenologists have shown some evolutionary change in their ideas since the days of Kraepelin (1919) who, even though initally conceptualizing schizophrenia as a defect state which was progressively deteriorative in nature, eventually had to reconcile himself to the fact that thirteen percent of his schizophrenic patients recovered. Although not totally rejecting the concept of deteriorating schizophrenia, more recently, productive features of the disorder have also become accepted as pathognomonic of the disorder (American Psychiatric Association, 1987; Feigner et al., 1972). While American psychiatry has clearly recognized the importance of subtyping, disagreement remains as to the best nosological system. Andreasen and Olsen (1982) have pointed out that several different nosological systems of schizophrenia have been widely utilized over the years. These include:

1) Those which emphasized cross-sectional phenomenology such as the more traditional Kraepelin-Bleulerian

division into hebephreic, catatonic, paranoid, and simple which still forms the basis for DSM III-R (APA,1987) subtyping of schizophrenia.

2) Other cross-sectional subdivisions including:
   schizoaffective bs. nonaffective
   paranoid vs. nonparanoid
3) Subtypes which emphasize the longitudinal course of the disorder including:
   acute vs. chronic
   process vs. reactive
   good vs. poor prognosis

The search for a classification system with documented prognostic capabilities as well as obvious relevance to treatment in addition to an etiological understanding of the disorder has led to the revival by Crow (1980a,1980b) in England and Andreasen (1982; Andreasen & Olsen, 1982) in the United States of an earlier proposition by Hughlings-Jackson (1931) that there may be two homogeneous subtypes within the schizophrenic disorder. The Positive (Type I) schizophrenic exhibits the more productive or florid symptoms while the Negative (Type II) schizophrenic manifests symptoms of the defect variety. Several differences between these two groups have been outlined by Crow (1980a) [Table 1].

Table 1

Positive and Negative Schizophrenic Syndromes

	Type 1	Type II
Characteristic Symptoms	Hallucinations	Affective Flattening
	Delusions	Poverty of Speech
	Thought Disorder	Loss of Drive
Intellectual Impairment	Absent	Sometimes present

(after Crow, 1980a)

Bleuler's dictum that schizophrenia actually represents a group of related disorders has recently been reiterated by Andreasen (1985):

> The diversity of schizophrenia suggests that the disorders grouped under the general term may in fact represent several different specific diseases that may differ in important ways [such as involvement of different neurotransmitter systems, different brain regions, or different etiological

agents] (p. 380).

One criticism of the positive-negative dichotomy has been the existence of a subset of patients who exhibit both positive and negative symptoms, the so-called "mixed" patient. While some believe that such patients represent a third subtype, other, more parsimonious, explanations have been forthcoming although none has achieved pre-eminence. These explanations include the following:

1) The coexistence of multiple causes of schizophrenia in some patients migh lead to a "mixed" phenomenological presentation.

2) Multiple involvement of different cerebral regions may, depending on the foci, result in a "mixed" symptom picture.

3) A "mixed symptom" picture may also be due to an imbalance of multiple neurochemical systems.

4) If one accepts the proposition that some patients evolve from a positive to a negative state over time, then it may be the case that the "mixed" patient is at an intermediary stage and a full blown negative syndrome has not yet developed (Andreasen, 1985, p. 231).

To this list one may add yet another possibility, that is, positive and negative subtypes may actually represent separate dimensions rather than homogeneous syndromes. Thus, a patient may present with negative symptoms and yet be predominantly positive in his phenomenology.

Given that the positive/negative approach to conceptualizing schizophrenia has been seriously examined for less than a decade and that a well validated phenomenological rating scale has only recently been developed, I would like to examine evidence in several areas relevant to this study which directly addresses a number of methodological flaws inherent in earlier studies of this phenomenon. These areas include:

1) The validity of positive and negative subgrouping in schizophrenia
2) An examination of relevant metabolic and structural abnormalities in the schizophrenic disorder
3) A review of studies demonstrating neuropsychological dysfunction in schizophrenia which may be of particular significance to positive and negative phenomenological presentation.

Phenomenology and Prevalence of Positive and Negative Subgroups

Kraepelin's influence on the development of diagnostic nonmenclature relevant to the diagnosis of schizophrenia was a long lasting one, influencing the conceptualization of the schizophrenic disease for over half a century. During that period, it was felt that the deteriorating clinical course of the disease was the cardinal feature distinguishing it from other psychiatric disorders. It was concern regarding the reliability of diagnosis, principally by the German phenomenologists during the middle of the twentieth century, that eventually led to a greater emphasis on productive symptomatology. Kurt Schneider (1957, 1959), one of the most influential representatives of the German phenomenological school, sought diagnostic criteria based on psychopathological manifestations that occurred frequently in schizophrenia and could be reliably evaluated by clinicians. Schneider gave diagnostic primacy to a few symptoms which he felt met this criteria. These "First Rank Symptoms" were regarded by him as pathognomonic of schizophrenia in the absence of known physical illness. Each of his first rank symptoms were productive ones with nonproductive symptoms being relegated to minor significance. Other, more recent, diagnostic systems such as the Diagnostic and Statistical Manual of Mental Disorders [DSM-III] (American Psychiatric Association, 1987), the Research Diagnostic Criteria [RDC] (Spitzer et al., 1987), the New Haven Schizophrenia Index (Astrachan et al., 1972) and the Carpenter-Strauss Criteria (Carpenter et al., 1973) have placed considerable importance on productive symptomatology without emphasizing a deteriorating course of illness.

Despite this reliance on productive symptoms in the diagnosis of schizophrenia, there has been an increasing tendency towards a narrowing of the concept of schizophrenia. As an example, the number of different subtypes has decreased from the DSM II to DSM III-R manuals. This collapsing of different diagnostic categories has been quite helpful for schzophrenia researchers who very often compare the performances of different subtypes with one another. Despite this trend towards fewer subtypes, it has become rather clear that phenomenological heterogeneity exists across these subtypes. Such heterogeneity has led to a revival of interest in the "defect" state such that both "defect" as well as productive symptoms are viewed as important in schizophrenia research. One of the results of this has been the revival of the positive/negative approach to conceptualizing schizophrenia.

The popularization of the positive/negative distinction has been of great heuristic value, leading to research aimed at examining whether this characterization would provide information germane to etiological, prognostic, and treatment hypotheses. Unfortunately, empirical work in this area has yielded mixed results due, in large part, to methodological flaws. These flaws, which have recently been elucidated in a review article by Kay and Opler (1987b), include small samples, imprecise or unstandardized rating instruments, different rating methods used across studies, lack of long-range follow-up, no control for differences in general severity of psychopathology, and no control for extrapyramidal symptoms (EPS) which could potentially interfere in the assessment of motor activity, affect, and verbal productions.

As listed in Table 1, the Positive (Type I or productive) Syndrome schizophrenic exhibits symptoms which may include delusions, hallucinations, thought disorder, and bizarre behavior while the Negative (Type II or defect) Syndrome schizophrenic exhibits apathy, withdrawal, poverty of speech, and blunted affect (Crow, 1980a; Strauss et al., 1974). In addition, the negative schizophrenic is believed to exhibit a poorer premorbid level of functioning, that is, demonstrates an earlier onset of symptomatology and psychosocial maladjustment. Thus, the negative subtype, believed to be the least responsive to treatment and to have a poorer prognosis, tends to exhibit premorbid social withdrawal and isolation (Cannon-Spoor et al., 1982; Gittelman-Klein & Klein, 1969). On the other hand, the positive schizophrenic usually demonstrates adequate premorbid psychosocial functioning and a more favorable response to neuroleptic treatment with periodic partial remission of symptoms. This method of conceptualizing schizophrenia has been considered useful in identifying relatively homogeneous subtypes within this disorder. The development and validation of the positive/negative dichotomy in schizophrenia will now be discussed.

Positive and Negative phenomenology

Much of the recent work on the positive/negative dichotomy in schizophrenia was originally based on Hughlings-Jackson's (1931) hierarchical conceptualization of cerebral functional organization. Jackson postulated that superordinate cerebral centers modulate by means of inhibiting subordinate ones with these subordinate centers providing the necessary "activation" for all brain functions. Lesions of subordinate centers thus result in an impairment of arousal and concommitant decrement of activity as well as responsivity in various brain centers. It has been pointed out that the basic factor in different disturbances is not necessarily a primary defect of the "proper function" of the affected area of the brain, nor does it necessarily lead to the total loss of this function. In many cases the function is merely depressed, and this is demonstrated by local disturbances in the neurodynamics of a particular function that is, a weakening or inadequate mobility of nervous processes or a weakening of internal inhibition. The effect of a generalized disturbance in the dynamics of nervous processes is felt primarily on those forms of cortical activity with the most complex organization. It follows then that it is the higher level of organization of mental processes which suffer most in this case and that one sees a depression of various forms of mental activity (Luria, 1973, 1980). The general behavioral manifestation of cerebral dysfunction of the subordinate "activation" centers lead to "defect" symptoms pathognomonic of the negative schizophrenic. Such symptoms include a lack of drive, anhedonia, decreased motor and speech activity, as well as social withdrawal. On the other hand, disturances at the higher superordinate centers generally result in disinhibition leading to unmodulated cerebral activity, disorganization, and "productive" symptomatology. Productive symptoms include disordered expression and thought bizarre perceptual experiences such as hallucinations, and active disturbances of affect. Thus positive symptoms are noted for their presence while negative symptoms are conspicuous for their absence, that is, the absence of goal-directed activity.

Interdisciplinary Studies

Relationship between clinical and CT Scan findings

As early as 1927, Jacobi and Winokur reported the use of pneumoencephalography (PEG) in the study of schizophrenia. While never a widely applied technique due to its incovenience and significant discomfort associated with the procedure, PEG studies nevertheless contributed a number of interesting findings regarding structural changes in the brain of schizophrenics. Weinberger and Wyatt (1982) have concluded from these findings that schizophrenics appeared to possess enlarged lateral ventricles, enlarged third ventricles, and widened cortical sulci. Of particular significance was the association of these findings with negative symptoms such as apathy or flattened affect as well as with cognitive impairment and poor outcome.

The development of computerized axial tomography (CT scan) has provided researchers with a noninvasive method of producing a composite picture of the brain which is very sensitive to structural abnormalities and cerebral atrophy. CT scan studies of schizophrenia have, in general, support the earlier PEG findings of increased cerebral abnormalities in schizophrenics when compared with a variety of normal and psychiatric controls. (Weinberger, 1982). Some of the abnormalities cited have included ventricular enlargement (Andreasen & Olsen, 1982; Andreasen & Smith, 1982b; Golden et al., 1980, 1982; Johnstone et al, 1976, 1978; Nasrallah et al., 1982a,b; Weinberger et al, 1979a, 1982), cortical atrophy (Golden et al., 1980, 1982; Rieder et al, 1979; Weinberger et al., 1979b), cerebellar atrophy (Weinberger et al., 1979b, 1980), and reversed cerebral asymmetry (Luchins et al., 1979, 1982). Of the above, ventricular enlargement is the most common abnormality found (Seidman, 1983). In most of these studies, ventricular size was measured by planimetry and a highly reliable ventricular-brain ratio (VBR) was determined. It is interesting to note that findings of increased VBR's in schizophrenics has been found to be independent of previous neuroleptic medication or dosage (Johnstone et al., 1976; Nasrallah et al., 1982b; Owens et al., 1985; Williams et al., 1985), ECT (Johnston et al., 1978; Schulsinger et al., 1984; Williams et al., 1985), sex, length of illness, or duration of hospitalization (Trimble & Kingsley, 1978; Weinberger et al., 1979a) or age (amongst schizophrenics) (Nasrallah et al., 1986; Obiols-Llandrich et al., 1986).

While Weinberger et al. (1979a) have demonstrated the existence of increased VBR's in nonchronic patients, chronic schizophrenics tend to have a higher rate of ventricular enlargement. Unfortunately, their sample was not phenomenologically differentiated according to positive and negative symptomatology and thus, while there are nonchronic schizophrenics who fall into the negative or defect subtype (Lindenmayer et al., 1984), it is impossible to determine whether Weinberger's acute sample with ventricular enlargement were members of the negative subtype in which case one would expect to see increased VBR's. The significance of these stuides is that CT scan abnormalities, which have been estimated to run at between 20-35% in schizophrenia, have been found to correlate highly with neuropsychological deficits (Donelly et al., 1980; Golden et al., 1980, 1982; Johnstone et al., 1976, 1978; Rieder et al., 1979) and with poor premorbid adjustment (Weinberger et al., 1980). It is important to note that greater neuropsychological deficits and poor premorbid adjustment are two of the primary characteristics of the Type II or negative schizophrenic (Andreasen, 1985). Those patients with ventricular enlargement were also found to demonstrate predominantly negative phenomenologies including alogia, affective flattening, avolition, and anhedonia as well as poorer response to treatment with neuroleptics. The fact that Weinberger et al. (1982) found evidence of abnormalities (i.e. increased VBR's) in young nonchronic first episode schizophrenics in addition to those who were chronic patients suggests a possible ontogenetic component to the course of illness in those schizophrenics with CT scan abnormalities.

This is because the rapid development of ventricular enlargement would typically elicit neurologic symptoms and possibly signs of increased intracranial pressure (Nasrallah et al., 1986; Owens et al., 1985; Weinberger et al., 1982). Thus, it is more likely that an abnormal neuropathological process occurs earlier in development (Weinberger et al., 1980; Cannon-Spoor et al., 1982). This may, in turn, be reflected in incomplete cognitive development and concommitant impaired performance across neuropsychological tests. In addition, several other clinically relevant factors have been found to be associated with ventricular enlargement. These include poor premorbid adjustment, poor work history, poor response to neuroleptic treatment, a lower incidence of positive symptoms, and an increased prevalence of negative symptoms (DeLisi et al., 1983; Weinberger et al., 1980; Williams et al., 1985).

Relationship between clinical and PET Scan /Regional Cerebral Blood Flow (rCBF) studies

Another recent technological advance in neuroimaging has been Positron Tomography (PET scanning), a technique making possible direct measurement of regionally specific glucose metabolism. Besides its extreme sensitivity, PET scanning has the additonal advantage of being capable of making its measurements in any region of tissue or structure of particular interest by utilizing tomographic techniques. Measurements derived from deep structures remain accurate despite being made non-invasively with external detectors. The development of technologies capable of measuring regional cerebral blood flow (rCBF) and local cerebral glucose metabolism (PET scan) has led ot a number of studies of cerebral metabolism in schizophrenia. These techniques have made it possible to study localized cerebral dysfunction given that metabolic and functional activity of local cerebral tissue, measured by glucose and oxygen consumption, has proven to be highly correlated with regional cerebral blood flow (Ingvar, 1976; Ingvar & Franzen, 1974; Matthew et al., 1981). Several independent groups have reported a decrease in frontal as compared to posterior metabolic activty in chronic schizophrenic patients when compared with controls (Ariel et al., 1983; Berman et al., 1984; Buschsbaum et al., 1982; Farkas et al., 1984; Widen et al., 1981; Wolkin et al., 1985). These studies corroborate earlier work demonstrating 'hypofrontality' in schizophrenics as opposed to normal control groups (Ingvar & Franzen, 1974; Ingvar, 1976). In earlier studies, it was found that, when mean cerebral blood flow (CBF) was measured, those patients who exhibited symptoms which would fall into what today is considered a predominately positive or Type I (productive) phenomenological cluster had high CBF's whereas those exhibiting negative or Type II symptoms had the lowest CBF's (Hoyer & Osterreich, 1975; Ingvar & Franzen, 1974; Franzen & Ingvar, 1975, Ingvar, 1976).

These findings have been interpreted as supporting an inverse relationship between increasing cognitive disturbance and rCBF in frontal regions (Ingvar, 1976). This "hypofrontality" was also found to be independent of age or neuroleptic use (Ingvar, 1976). Thus, subjects exhibiting predominantly negative symptoms may be expected to perform more poorly than patients exhibiting predominantly positive symptoms on tasks used to assess anterior/executive functioning.

While the application of PET scan technology to the study of psychiatric disease remains in its infancy, several interesting findings have been forthcoming. Specifically, a number of PET studies have reported lower levels of frontal activation in schizophrenics when compared with normal controls (Buchsbaum et al., 1982; Farkas et al., 1984; Gur, 1982; Widen et al., 1981). More recently, Buchsbaum et al. (1984) and Farkas et al. (1980) reported that patients with schizophrenia exhibited a decreased antero-posterior glucose gradient. Data also indicates that findings of abnormal frontal lobe metabolism in schizophrenia are not likely to be the result of neuroleptic treatment (Buchsbaum et al., 1982). One of the most comprehensive PET studies of schizophrenia has emphasized frontal and greater left than right hemisphere dysfunction (Ingvar, 1976). Seidman (1983), citing Weinberger (1982), has summarized Ingvar's conceptualization of the results as follows:

> They (Ingvar et al., 1976) hypothesized that schizophrenics suffer from a fundamental deficit in activation because there is a defective frontal response to stimuli as well as a minimal resting frontal RcbF. They suggest that the primary disorder is an abnormal distribution of function cause by a defect in the nonspecific medio-thalamic, fronto-cortical projection system. There is a failure of brain-stem and limbic mechanisms to activate the frontal lobes (p.208).

Buchsbaum et al. (1982) believe this type of defect to actually reflect a cortical-subcortical dopaminergic dysfunction. Phenomenological differences in activation have also been reported. Specifically, Volkow and coworkers (1986) found that when schizophenic patients were characterized with respect to positive and negative symptoms, patients with predominantly negative symptoms exhibited relative lower metabolic activity during a visual task than did patients with predominantly positive symptoms.

Results have not been limited to lower frontal activation in schizophrenia. In a test-retest study, Wolkin et al. (1985) found significantly lower CMR_{gl} in the left temporal region in addition to the left frontal areas in their schizophrenic subjects as compared to a normal control group. In a study of 15 medicated schizophrenics and 25 control subjects (matched for age, sex, education, and socioeconomic status) during cognitive activity, Gur and coworkers (1979, 1983) found that the LH fails to activate more than the RH for verbal tasks in schizophrenics. However, there was a greater LH than RH increase for spatial processing tasks. Gur concluded that this dysfunction may be due to the relative failure of the LH to become active for verbal tasks and, instead, inappropriately "overactivates" to the spatial task.

In a follow-up study using the same paradigm as in her first study, Gur et al. (1985) included 19 unmedicated schizophrenics and 19 matched controls. Resting flows were found to be higher in the LH for schizophrenics ($p < .05$) with anterior flows being higher than posterior flows. During cognitive activity, schizophrenics demonstrated higher flows for the verbal than spatial tasks. When the effect of medication was examined, medicated schizophrenics were found to have more symmetric flows whereas, unmedicated schizophrenics had greater LH flows, more pronounced in the precentral regions. This finding is, of course, quite consistent with behavioral data which suggest LH overactivation in schizophrenics (Gur, 1978; Schweitzer et al., 1978). When both medicated and unmedicated schizophrenic subjects were further divided into low and high psychopathological severity groups with the Brief Psychiatric Rating Scale (BPRS), those patients with a greater degree of psychopathology had higher resting flows. When cognitive activation was introduced, this same group showed less increase in rCBF than the subjects with a lower degree of psychopathology. According to Gur et al. (1985):

> The findings of LH increased flows, even for the spatial task, supporting the hypothesis of LH overactivation, also raises the question of RH functioning in schizophrenia (p. 85).

She goes on to point out that the RH, in addition to its role in spatial processing, has been linked to attention and arousal. Several PET Scan studies of the RH role in the attentional functioning of schizophrenic subjects have revealed that subjects attending to stimuli demonstrate significantly higher RH laterality of metabolism as compared to normal controls (Reivich et al., 1983; Roland, 1982; Roland et al., 1982). These increases have been found to consistently occur within the inferior parietal cortex. Thus, the possibility is raised that schizophrenics display a dysfunction of RH input in their attentional network.

In summarizing a series of papers, Invar (1980) concluded that resting rCBF varies in relationship to the relative presence of positive or negative symptoms. In her review highest flows were found in schizophrenic patients with positive symptoms while lower rCBF was associated with patients exhibiting a predominance of negative symptoms. This had also been found by Hoyer & Oesterreich, (1975). In addition, increases in cognitive impairment correlated negatively with frontal flows. One would therefore assume that those patients presenting with a predominance of negative symptoms would exhibit a greater degree of neuropsychological deficits associated with anterior dysfunction than would patients who demonstrate a predominance of positive symptoms.

Although promising, it must be borne in mind that PET data have usually been collected on rather small samples and further studies utilizing larger sample bases are required before conclusive evidence is acquired. Nevertheless, its heuristic value in the study of schizophrenia is well recognized with major findings to date being consistent with the results of other studies utilizing different techniques.

Relationship between clinical and neuropathologic findings

When one examines the early Pneumoencephalographic (PEG) studies one finds, as is the case with postmortem neuropathologic studies, that schizophrenic cerebral abnormalities differ both qualitatively and quantitatively from other patient populations. As an example, these studies primarily reveal subcortical atrophy in schizophrenics whereas other patients with cerebral abnormalities had a tendency towards either focal disease or diffuse cortical rather than subcortical atrophy. In light of present interest in subtyping schizophrenia along the positive/negative dimension, those patients exhibiting the most severe PEG abnormalities tended to be those demonstrating negatve or defect symptoms (Asano, 1967; Haug, 1962; Huber, 1957). Specifically, these patients exhibited impaired cognitive functioning, affective blunting, an impaired capacity to work, poor social functioning, and a poor prognosis (Ansink et al., 1963; Haug, 1962; Huber et al., 1980; Huckman et al., 1975; Kiev et al., 1962; Lonnum. 1966; Matthews & Booker, 1972).

A number of post-mortem studies have revealed several neuropathological changes in the brain of schizophrenics including a widening of the corpus calloum (Rosenthal & Bigelow, 1972), cerebellar abnormalities (Weinberger et al., 1980), and cerebral atrophy (Asano, 1967; Ansink et al., 1963;

Haug, 1962; Huber, 1957; Luchins et al., 1979; Young & Crampton, 1974). These findings were independent of age, sex, drug treatment, and duration of the disorder.

While these cerebral changes may also be found in nonpsychotic individuals, such pathology tends to be quantitatively higher in schizophrenics. More recently, Brown et al. (1986) have reported neuropathological studies which indicate that, when brains of schizophrenic patients were compared with brains of nonpsychiatric patients and patients with affective illness, the schizophrenic patients had brains that (1) were 6% lighter; (2) had larger lateral ventricles in the anterior and temporal horn cross section; and (3) had significantly thinner parahippocampal gyri, by 11%. This report is consistent with CT findings of ventricular enlargement in schizophrenic patients as a group.

Neuropsychological Studies

While Goldstein (1978) points out that neuropsychological deficits found in studies of psychiatric patients were frequently considered to be secondary to psychodynamic disturbances, many of these stuides were flawed by criterion bias. Very often, these earlier studies of psychiatric patients utilized a neurological examination in determining the presence or absence of "organicity." If included at all, neuropsychological evaluation was often limited to a single instrument.

Within the past decade, neuropsychological and biobehavioral studies have provided evidence supporting the contention of cerebral dyfunction in schizophrenia. There now exists a body of evidence which suggest that chronic schizophrenics exhibit neuropsychological profiles consistent with cerebral dysfunction (Carr & Wedding, 1984; Goldstein & Halperin, 1977; Heaton et al., 1981; Klonoff et al., 1970; Malec, 1978: Taylor & Abrams, 1984). Other studies have documented similarities in performance between chronic schizophrenics and patients with neurologically diagnosed brain damage (Heaton et al., 1981; Goldstein, 1978; Malec, 1978). When combined with results of studies utilizing modern neuroimaging techniques, this evidence has led to wide acceptance of the notion that many chronic schizophrenic patients do indeed suffer from organic dysfunction.

While the results of many earlier studies utilizing psychological tests were marred by a number of potentially confounding variables, they were generally consistent in finding that chronic schizophenics performed in a manner which was indistinguishable from patients with neurologically diagnosed brain disease. Specifically, during testing many chronic schizophrenics perform at levels which fall below the cutoff scores for the identification of brain damage. In addition, neuropsychological impairments demonstrated by chronic schizophrenics have generally been consistent with bilateral and diffuse cerebral dysfunction rather than with localized cerebral compromsie (Bilder, 1985; Davison & Bagley, 1969; Flor-Henry, 1976, Flor-Henry & Yeudall, 1979; Flor-Henry, 1983). However, many such reports have proven inconsistent in their localization of regionally specific cerebral dysfunction with some being difficult to interpret because of methodological flaws. Despite this, the proposal has been made that schizophrenics demonstrate greater dominant than nondominant cerebral dysfunction (Flor-Henry, 1969, 1976, 1979; Flor-Henry, 1983). Evidence supporting this proposition has come from studies demonstrating schizophrenic-like psychosis in left unilateral temporal lobe epilepsy (Flor-Henry, 1969); in cases of left unilateral brain insult (Davison & Bagley, 1969); and from patients with affective psychosis (Flor-Henry, 1976). In addition to the dominant hemisphere impairment hypothesis, evidence in support of an anterior dysfunction also comes from studies of cerebral metabolism (Buchsbaum et al., 1982; Ingvar, 1976), electroencephalography (Serafetinides, 1972, 1973; Coger et al., 1979), evoked potentials (Buchsbaum et al., 1979), as well as electrodermal, tachistoscopic, dichotic listening, and lateral eye-movement studies (see eg., Taylor et al., 1981; Tucker, 1981; for reviews). However, conflicting results have been reported (Newlin et al., 1981) and alternative interpretations of these findings have been offered (eg., defects of interhemispheric transfer [Beaumont & Dimond 1973; Green, 1978]). Controversy has also centered on whether the dysfunction attributed to the left hemisphere reflects hypo- or hyperactivation (Gur, 1979; Gruzelier, 1981).

One possible explanation for the lack of consistent findings in localizing regionally specific areas of cerebral dysfunction has been the heterogeneity of the schizophrenics studied and the possible interaction of phenomenological presentation with performance on cognitive tasks. It is possible, for example, that cerebral regions which are dysfunctional could be isolated in specific subgroups of schizophrenic patients. Such subgroups might demonstrate different patterns of neuropsychological deficits which would be of localizable significance. It is unfortunate that there have been few systematic studies of neuropsychological differences between schizophrenic patients which have been subgrouped with a well standardized phenomenological instrument.

In addition to increasing interest in examining regionally specific deficits, the course of neuropsychological deterioration in schizophrenia has attracted attention. Up until recently, the course of intellectual decline in schizophrenia has received little empirical attention, possibly because the major focus of research in this area was simply delineating cognitive impairment. While several earlier longitudinal studies cited evidence of little or no cognitive deterioration in schizophrenia following its onset (Klonoff et al., 1970; Foulds & Dixon, 1962; Hamilton, 1963; Hamlin & Ward, 1973), others have suggested that significant deterioration may occur in subgroups of patients (Haywood & Moelis, 1963; Smith, 1964). One of the reasons often cited in the literature for the lack of definitive evidence in this area has been the reported paucity of studies comparing pre- and post-morbid levels of cognitive functioning (Rieder et al., 1977; Oltman et al., 1978; Watt, et al., 1982). Despite this, there are several retrospective analyses of school and/or army intelligence tests which indicate that individuals who later developed schizophrenia had performed more poorly than their peers or siblings who remained well (Offord, 1974; Lane & Albee, 1965; Miner & Anderson, 1958; Watt & Lubensky, 1976). However, once again, these studies failed to subgroup patients according to phenomenological presentation.

While studies of impaired cognitive functioning in schizophrenia abound, studies of cognitive developmental failure in schizophrenia are fewer. As early as 1937 Langfeldt pointed out the importance of developmental issues in understanding the stable, treatment resistant aspects of schizophrenia in distinguishing nuclear-process (poor prognosis) and reactive (good prognosis) subtypes. Despite psychopharmacological advances, those characterized by poor premorbid admustment and early conceptual deficits, reportedly schizophrenics presenting with a predominantly negative phenomenology (Kay & Opler, 1987a), have continued to demonstrate less successful recovery (Albee, Lane, & Reuter, 1964; Putterman & Pollack, 1976; Spohn, Lacoursiere, & thompson, 1977). The finding that conceptual deficits are resistant to antipsychotic drug treatment (Chapman, Cameron, Locke, & Pritchett, 1975) coupled with the necessity of intact cognitive functioning for adequately dealing with the problems of everyday life (Yozawitz, 1986) may help to explain the significant recidivism rate amongst schizophrenics discharged from hospitals. This may also explain the poorer prognosis of negative subtype patients. That is, if they demonstrate imcomplete cognitive development as has been proposed (Kay, Opler, & Fiszbein, 1986; Opler et al., 1984) it may be that they are less well equipped cognitively to handle the demands of everyday living.

Hypotheses

Based on the literature reviewed, it is hypothesized that subjects dichotomously assigned to positive and negative phenomenological groups will both appear cognitively impaired based on their performance on neuropsychological tests. However, the negative group as well as those displaying a greater degree of negativity than positivity will demonstrate significantly more impairment than the positive group on those tests which assess anterior functioning. Subject performance on cognitive developmental tasks will be such that patients placed into the negative group will demonstrate less complete cognitive development than those in the positive group. During dimensional analysis, a subject's degree of cognitive development will vary as a function of the relative prevalence of positive and negative symptoms. Specifically, the greater his negative scale score, the lower his scores will be on cognitive developmental tasks.

In addition, the relative negativity and positivity of subjects will be related to subject control variables such that either negative group membership or a greater degree of negativity versus positivity will be associated with an earlier age of onset, less education, a greater duration of illness, longer hospitalization, and a greater degree of motor abnormalities.

Next, the general intellectual capacity and cognitive developmental performance of subjects will be positively correlated to age of onset and educational attainment.

Finally, both positive and negative groups will display a disturbance of affect such that the negative group as well as a greater degree of negativity will be associated with emotional unrelatedness and expressive immobility. The positive group and a greater degree of positivity, on the other hand, will be associated with inappropriateness of affect.

Methods

Subjects

Psychiatric inpatients at Bronx Psychiatric Center (BPC), an urban medical school affiliated psychiatric facility of the New York State Office of Mental Health, who were between the ages of 18 and 60 and have satisfied DSM-III-R criteria for a diagnosis of schizophrenia served as potential experimental subjects to be screened for this study. Subjects received neuroleptic medication at the time of clinical and neuropsychological examination and were maintained on chlorpromazine during their involvement in this study. Chlorpromazine (CPZ) equivalence was determined for those subjects who, for clinical reasons, could not be maintained on CPZ. Exclusionary criteria for this study included neurological disease, a history of having sustained a head injury resulting in coma or significant unconsciousness, concurrent metabolic illness known to adversely affect mood or cognitive processing, a long term history of chronic alcholism extending to within a year of involvement in this study, a developmental history of mental retardation, and electroconvulsive therapy (ECT) within two years prior to protocol screening. Prior to the initiation of this study, it was decided that the results would be based on the first 35 experimental subjects admitted to this protocol. Of these 35 subjects, three were judged too psychotic to cooperate with the experimental procedures and two other subjects refused all testing after they had given informed consent. Thus, the results are based on the first 30 subjects admitted to the protocol who were able to cooperate with the procedures. Among these subjects, not all information could be obtained for every individual due to the inconsistency of their cooperation across all measures. Basic demographic, historical, and treatment characteristics of the sample are shown in appendix 1.

Procedures

Screening and selection

Prospective experimental subjects were identified by staff psychiatrists at BPC or by Psychiatry research fellows from the Department of Psychiatry at the Albert Einstein College of Medicine who were assigned to the Schizophrenia Research Unit at BPC. One of these research fellows or staff psychiatrists explained the nature of the research protocol procedures to potential subjects and obtained informed consent. Satisfaction of inclusion and exclusion criteria were determined on the basis of a clinical interview conducted by not less than two psychiatrists, chart review, and a physical examination which included a neurological screening examination. It should be noted that this research study was reviewed and approved by the

Institutional Research Review Boards of BPC and the New York State Office of Mental Health.

Outline of assessment procedures

Following admission to the protocol and subsequent transfer to the Schizohrenia Research Unit, each patient was permitted one to two weeks in order to acclimate himself to the unit. After four to five weeks and placement on CPZ, the patient underwent clinical phenomenological evaluations, a motor evaluation to evaluate for the presence of drug-related abnormal motor functioning which could influence other testing, cognitive developmental assessment, and neuropsychological examination. These procedures were performed within three weeks of one another. Following completion of the study, each patient was given an opportunity to participate in an informing session. Results of the evaluations were discussed with appropriate unit staff members prior to such sessions.

Clinical Assessment

In addition to a clinical interview, chart reveiw, and history taking, the clinical evaluation included ratings on several interview scales. These included the Positive and Negative Syndrome Scale [PANSS] (Kay, Fiszbein, & Opler, 1987), the Scale for the Assessment of Positive Symptoms (Andreasen, 1984), the <u>Scale for the Assessment of Negative Symptoms</u> (Andreasen 1983), and the <u>Manifest Anxiety Rating Scale</u> [MARS] (Albert & Rush, 1983).

All subjects were rated on both positive and negative symptomotology and general degree of psychopathology by a minimum of two psychiatrists utilizing the PANSS which was developed by Kay et al. in a series of previously published studies (1987, 1988). The PANSS encompasses symptoms from the Brief Psychiatric Rating Scale [BPRS] (Overall & Gorham, 1962) and the Psychopathology Rating Scale [PRS] (Singh & Kay, 1975a). The PRS was used in order to provide a more robust assessment of negative features by evaluating subjects on symptoms not included on the BPRS. The PANSS was chosen as the instrument to be used in the evaluation of positive and negative symptoms in this study because it addressed the limitations shared by other scales. These limitations include inadequately defined terms; lack of operational criteria; inadequate reliability or validity data; an unequal number of items representing positive and negative syndromes; measures of the relative severity of positive and negative symptoms; measurement of the relative preponderance of positive vs. negative symptoms; and finally, many of these scales did not include a measure of general psychopathology and its possible influence on the severity of positive and negative syndromes

(Kay, Fiszbein, & Opler, 1987). Standardization of the PANSS on almost 200 DSM-III diagnosed schizophrenics examined for several studies has yielded an interrater reliability of between 0.83 and 0.87 for all scales, with correlations being highly significant ($p < .001$) (Kay et al., in press). In addition, internal reliability was examined by the alpha coefficient method with overall coefficients being 0.73 and 0.83 for the Positive and Negative Scales respectively. The mean-item total correlations were 0.62 and 0.70 respectively. Cross-correlations have been found to be nonsignificant at 0.17 and 0.18. Finally, the General Psychopathology Scale also showed a satisfactory alpha coefficient of 0.79 in addition to a split-half reliability coefficient of 0.80. These observed values have been reported as being significant beyond $p < .001$ (Kay et al., 1986).

The actual method of clinical evaluation consisted of a 40-50 minute semi-structured interview conducted by a psychiatrist in the presence of additional professional staff (psychologists and/or psychiatric social workers) raters who had received formal training in the instrument. The purpose of this interview was to observe affective, motor, cognitive, attentional, and communicative functions. The interview was broken down into four major phases which have been described by Kay, Opler, & Fiszbein (1986) as follows. In the first 10-15 minutes, patients were encouraged to discuss their history, circumstances surrounding their hospitalization, their current life situation, and their symptoms. The interviewer at this point assumed a nondirective, unchallenging posture in order to observe, as unobtrusively as possible, the nature of thought processes and content, judgement and insight, communcation and rapport, and affective and motor responses.

Deviant material from the first segment of the interview was probed during the second phase, lasting another 15 minutes, by the use of nonprovocative but leading questions (e.g., Do you feel that you can trust most people that you know? Do you have some unusual abilities? Do you sometimes have strange experiences?). The object was to measurably assess productive symptoms which could be judged from patients's report, such as delusional themes, suspiciousness, and hallucinations. For this purpose, the interviewer attempted to establish the frequency and severity of the symptoms, which were generally weighted according to their disruptive impact on daily functioning.

The third and most focused phase of the interview, requiring another 10 minutes, involved a series of specific questions to secure information on mood state, anxiety, orientation to three spheres, and abstract reasoning ability. The evaluation of abstract reasoning, for example, consisted of a range of questions on concept formulation (e.g., How are a train and bus alike?) and proverb interpretation, which could be varied in content when using the PANSS for repeated assessment.

After all the essential rating information was obtained, the final 10 minutes of the interview were used for more directive and forceful probing of areas in which the patient appeared defensive, ambivalent, or uncooperative. For example, a patient who had avoided forthright acknowledgment of having a psychiatric disorder might be challenged for a decisive statement. In this last phase, therefore, the patient was subjected to greater stress and testing of limits, which was thought to be necessary in order to proceed beyond the social demand characteristics inherent in the interview situation and to explore susceptibility to disorganization.

The interview procedure thus afforded raters an opportunity to observe physical manifestations (e.g., tension, excitement, blunting of affect), interpersonal behavior (e.g., poor rapport, inattention, uncooperativeness), cognitive-verbal processes (e.g., conceptual disorganization, stereotyped thinking, lack of spontaneity and flow of conversation), thought content (e.g., grandiosity, somatic concern, delusions), and response to specific lines of questioning (e.g. anxiety, disorientation, depressed mood). Following this semi-structured interview, subjects wiere rated on all clinical scales while utilizing guidelines available in the PANSS manual.

Data gathered during this interview was then applied to the PANSS (Kay, Fiszbein, & Opler, 1987), a 30-item, seven-point rating instrument which adapted 18 items from the BPRS (Overall & Gortham, 1962) and 12 items from the PRS (Singh & Kay, 1975a). It should be noted that each item on the PANSS is accompanied by a specific definition as well as detailed anchoring criteria for all seven rating points, representing increasing levels of psychopathology: 1-absent, 2 minimal, 3-mild, 4-moderate, 5-moderately severe, 6-severe, and 7-extreme [Table 2].

In order to provide a measure of criterion validity of the clinical phenomenological assessment of positive and negative syndromes, the Scale for Assessing Positive Symptoms [SAPS] (Andreasen, 1984) and the Scale for the Assessment of Negative Symptoms [SANS] (Andreasen, 1983) were employed simultaneously with the PANSS by the same raters. The SANS contains 30 items, twenty-five of which are ratings of individual symptoms, with the other five items being "global" ratings in each of five symptoms complexes (alogia, affective flattening, avolition/apathy, anhedonia/asociality, and attentional impairment). A validation study of the scale demonstrated interrater reliabilities of between .58 and .88.

Table 2

The Positive and Negative Syndrome Scale (PANSS)

<u>Positive Scale</u>

P1. Delusions

P2. Conceptual disorganization

P3. Hallucinatory behavior

P4. Excitement

P5. Grandiosity

P6. Suspiciousness

P7. Hostility

<u>Negative Scale</u>

N1. Blunted affect

N2. Emotional withdrawal

N3. Poor rapport

N4. Passive-apathetic social withdrawal

N5. Difficulty in abstract thinking

N6. Lack of spontaneity & flow of conversation

N7. Stereotyped thinking

(Kay, Fiszbein, & Opler, 1987)

The SAPS contains 38 items, thirty-four of which are ratings of individual symptoms, with the other four itmes, as is the case with the SANS, being "global" ratings in each of four symptom complexes (hallucinations, delusions, bizarre behavior, and positive formal thought disorder).

Since positive and negative symptomatology may be related to total psychopathology, the General Psychopathology Scale [GPS] (Kay, et al., 1986a) was also be administered. As previously stated, in developing the PANSS, 30 items were derived from the BPRS and PRS. Items identifying seven positive symptoms and seven negative symptoms comprise the first two parts of the PANSS while the remaining 16-items were incorporated into the GPS [Table 3], whose reliability and criterion-related as well as predictive validity have been established (Kay et al., 1986a). Scoring of the GPS is based on a seven point scale ranging from absent (score=0) to extreme (score=7). The potential range of scores is from 16 to 112 with these scores being convertible to percentile ranks.

Given that impaired affect has been considered one of the hallmarks of the "defect state" in schizophrenia (Feighner et al., 1972) and there is evidence supportive of this in the literature (Opler et al., 1984), a detailed assessment of affect was conducted utilizing the Manifest Anxiety Rating Scale [MARS].

Table 3.
General Psychopathology Scale (GPS)

Somatic concern
Anxiety
Guilt feelings
Tension
Mannerisms and posturing
Depression
Motor retardation
Uncooperativeness
Unusual thought content
Disorientation
Poor attention
Lack of judgement and insight
Disturbance of volition
Poor impulse control
Preoccupation
Active social avoidance

(Kay, et al., 1986a)

The MARS is a 15-item scale modified from the procedure developed by Alpert and Rush (1983) which evaluates general areas of communicative movements, mobility, and the congruence of feelings and thoughts. Each of the 15 items on the scale is rated on a 4-point severity scale, each withdescriptive anchoring points along with a range from 0 (normal) to 3 (extreme pathology). Principal component analysis has identified three factors underlying the scale: emotional unrelatedness (mean loading = 0.80), expressive immobility (0.71), and inappropriateness of affect (0.60) [Table 4].

Motor Abnormality Assessments

The prevalence of extrapyramidal symptoms were examined for their possible influence on judgements of negative and positive symptoms as well as on performance on motoric tasks during neuropsychological and cognitive developmental assessment.

Following a complete examination, one or more psychiatrist rated subjects using the 10-item Abnormal Involuntary Movement Scale [AIMS] (National Institute of Mental Health, 1974) which assesses the presence and severity of movement disorders involving the face, mouth, extremities, and trunk. The AIMS was included as a measure of tardive dyskinesia. The 7-item Extrapyramidal Rating Scale [EPS] (Alpert, et al., 1978), similar to Borison's Scale for Recognizing Acute Extrapyramidal

Table 4.

Manifest Affect Rating Scale (MARS)

Communicative Movements

1. facial expression
2. expressive gestures
3. vocal emphasis
4. eye contact
5. global rating of relatedness

Mobility

6. spontaneous noncommunicative movements
7. speech rate
8. response latency
9. voice level
10. lability
11. global rating of mobility

Inappropriateness of Feelings of Thought Content

12. silly affective tone in relation to content of discourse
13. angry affective tone in relation to content of discourse
14. sad affective tone in relation to content of discourse

continued

Table 4 (continued)

Manifest Affect Rating Scale

15. spontaneity of thought content

(Alpert & Rush, 1983)

Symptoms [EPS], will also be completed as an evaluation of bradykinetic and parkinsonian drug reaction. Such reactions were rated along seven dimensions: abnormal gait (stooping, loss of associated movement, shuffling, propulsion), rigidity (resistance to passive stretch, cogwheeling), tremor of extremities (including choreiform movements and pillrolling), bizarre movements (torticollis, facial grimace, tongue tremor, tics, oral movements), expression (masked facies, dysarthric speech, loss of volume, loss of inflection), restlessness (constant walking, rocking, chewing, sitting), and reduced motor activity (fatigue, slowness, weakness, inactivity). Ratings on both the AIMS and ERS range from 0 (no abnormality) to 4 (severe) and cover a wide spectrum of abnormal movements.

Neuropsychological Assessments

All neuropsychological testing of subjects were performed by this investigator. Although being aware, a priori, that all subjects were diagnosed schizophrenics, this investigator remained blind as to the results of both the clinical interview and clinical scales. The neurpsychological component of this study examined three general factors germane to the study of cognition. These factors included general indices of cognitive integrity, hemispheric dominance, and the assessment of specific cognitive dimensions which was viewed as the central component of this neuropsychological study. The neuropsychological test protocol designed for use in this study will require approximately six hours to complete. Tests were administered in a randomized order over three sessions with each session lasting two hours. Sessions were limited to two hours in order to avoid a fatigue effect. In addition, subjects were allowed breaks at their request in order to insure cooperation; however, intratest breaks were not permitted.

Selection of neuropsychological tests

Two of the most popular batteries, the Halstead-Reitan Battery (HRB) and the Luria Nebraska Neuropsychological Battery (LNNB) have not been proven capable of isolating patterns of specific regional brain dysfunction. While able to discriminate the presence of "organicity" and severe lateralized dysfunction, the HRB was not originally designed to directly assess the integrity of various functional systems within the brain (Heaton, et al., 1981; Tsushima & Wedding, 1979; Walsh, 1987). It is also lacking in its capacity to adequately assess memory and language functions. The LNNB, on the other hand, is crudely based on Luria's neuropsychological tasks (Luria, 1973). (Akhutina & Tsvetkova, 1983; Spiers, 1981). Spiers (1981) has said of the LNNB that:

> It is not these items, per se, but the manner in which Luria made use of them as a means of testing hypotheses concerning various abilities, deficits, or functions which is his method and his unique contribution to neuropsychological assessment. Consequently, the incorporation of items drawn from Luria's work into a standardized test should not be interpreted to mean that the test is an operationalization or standardization of Luria's method (p. 339).

Neuropsychological investigators have found that the LNNB does not assess any single discrete neuropsychological function in detail and should be consi dered diagnostically unreliable (Adams & Brown, 1980; Crosson & Warren, 1982; Delis & Kaplan, 1983). While the LNNB does indeed discriminate between brain-damaged subjects and normal controls at better than chance levels, once again, many collections of assorted cognitive tests would do the same. In addition to the HRB and the LNNB, there are neuropsychological test batteries, such as the Boston Diagnostic Aphasia Examination [BDAE] (Goodglass & Kaplan, 1983), which were designed to evaluate specific cognitive dysfunctions. While certain subtests of the BDAE and other test batteries were incorporated into the neuropsychological protocol of this study, none of them were considered approriate in their entirety.

In order to assemble those tests most pertinent to this study, a list of cognitive functions and functional brain regions were generated. Tests, both published and those widely accepted within the clinical and experimental literature, which fit this list formed the neuropsychological test battery. While many tests of cognition involve multiple functions, those tests were chosen which tend to be generally specific to a particular cognitive dimension. In addition to assessing general cognitive integrity and handedness, the neuropsychological test battery for this study was designed to evaluate the following cognitive dimensions: executive, sensory-motor, linguistic, visual-spatial, and memory. Once again, each of these dimensions was examined by tests known to be both sensitive and specific to that particular dimension. Also relevant to the inclusion of a particular test into the protocol were established validity within the literature; adequate reliability; and, instructions as well as task demands which were not overly complex. By necessity, these guidelines were compromised within reasonable limits in the selection of a few tests which are particularly well suited to a specific cognitive dimension. A complete listing of tests comprising the neuropsychological protocol for this study are listed in Table 5 by both superordinate and suborinate categories. Also listed for each test are both the general cognitive dmension as well as the specific aspect of that particular dimension addressed by the test.

One should note that the uneven emphasis attached to various cognitive dimensions within the neuropsychological test battery was largely influenced by reports in the literature. Specifically, it was decided, as an example, to emphasize tests of executive functioning in the design of the battery in view of existing literature linking impairments of executive processing and schizophrenia (Mirsky, 1969; Seidman, 1983; Smith, 1964) as well as reports of "hypofrontality" in schizophrenia (Franzen & Ingvar, 1975; Ingvar, 1976).

Description of neuropsychological measures

A description of the neuropsychological measures to be employed in this study is listed below by dimension:

General Indices of Cognitive Integrity

Wechsler Adult Intelligence Scale-Revised:

The WAIS-R is a carefully standardized battery composed of a number of distinct subtests which measures general intellectual capacity (Wechsler, 1958, 1981; Zimmerman et al., 1973). The battery consists of eleven different subtests, six of which were classified by Wechsler (1955) as "Verbal" tests and the other five as "Performance" tests. The "Verbal" subtests include Information, Comprehension, Arithmetic, Similarities, Digit Span, and Vocabulary with the "Performance" subtests being Picture Completion, Picture Arrangement, Block Design, Object Assembly, and Digit Symbol. The WAIS-R battery takes approximately one and one-half hours to administer and yields a Verbal IQ, Performance IQ, and a Full Scale IQ. It has also been found to be a highly reliable instrument, with reliability coefficients of .97 for the Full Scale IQ and in the .90's for the eleven subscales.

Wechsler Memory Scale:

The Wechsler Memory Scale was included in this battery as a general indice of cognitive integrity, given its reported comparability with overall intellectual capacity (Wechsler, 1945). The scale includes seven subtests with a subject's total score being arrived at by summing all subtest scores and adding a constant assigned for the age group into which a subject falls.

While all seven subtests will be administered, the three which are particularly relevant to this study have been included under appropriate subordinate cognitive categories (see Table 5). Those three will be described in detail.

The Mental Control Subtest is included as a measure of sequencing ability. This subtest requires a patient to: (1) count backwards from 20 to 1; (2) recite the alphabet; and (3) count by 3's from 1 through 40. Each of these tasks is timed with subjects receiving a preset score for a correct performance on each of the three tasks. One error is allowed with two or more errors yielding a score of 0 for that particular subtest. Subjects are able to receive extra credit for a speedy correct response. The Logical Memory Subtest involves free recall immediately following auditory presentation of each of two paragraphs. Paragraph A contains a total of 24 memory units or "ideas" with Paragraph B containing 22. Subjects obtain one point per "idea" recalled with his total score being the mean number of ideas recalled on both paragraphs. The Paired Associates Subtest involves presenting 10 stimulus words, each of which is paired with a specific response word. Following presentation of the 10 pair list, the subject is given one of the stimulus words and is asked to recall the particular response word associated with it. Of the 10 word pairs, six are high frequency paired associates [easy associates] (e.g., north-south) with the remaining four being low frequency paired associates

Table 5

Neuropsychological Research Assessment Battery

<u>General Indices of Cognitive Integrity</u>

Wechsler Adult Intelligence Scale-Revised

Wechsler Memory Scale

Raven's Progressive Matrices

<u>Test of Cerebral Dominance</u>

Annett Hardedness Questionnaire

<u>Specific Cognitive Dimensions</u>

<u>Executive Processing:</u>

Initiation: Verbal Fluency Tests

Sequencing: Trail-Making Test, Parts A & B; Mental Control Subtest (WMS)

Attention & Set: Letter Cancellation Test; Stroop Color-Word Test

Categorical Set-Shifting: Wisconsin Card Sorting Test

continued

Table 5 (continued)

Neuropsychological Research Assessment Battery

Sensory-Motor Processing:

Visual-Motor Speed & Coordination: Purdue Pegboard Test

Skilled Organized Movements: Boston Apraxia Test

Constructional Ability: Stick Construction Test (BDAE)

Somatosensory Processing: Single & Double Simultaneous (Face-Hand) Stimulation Test

Linguistic Processing:

Phonetic Processing: Wepman Auditory Discrimination Test

Lexical Processing: Visual Confrontation Naming Test (BDAE)

Syntactic Processing: Token Test (NCCEA)

Visual Spatial Processing:

Categorical Perception: Hooper Visual Organization Test

Non-Categorized Perception: Benton Facial Recognition Test

Directional Orientation: A Standardized Road Map of Direction Sense

continued

Table 5 (continued)

Neuropsychological Research Assessment Battery

<u>Memory Processing:</u>

Verbal Memory: Buschke Selective Reminding List Learning Test (Mixed List); Paired-Associate Learning (WMS); Logical Memory Test (WMS); Sentence Repetition Test (NCCEA)

Visual-Spatial Memory: Benton Test of Visual Retention (Admin. A); Benton Test of Visual Rentention-Recognition Form

WMS:	Wechsler Memory Scale
BDAE:	Boston Diagnostic Aphasia Examination
NCCEA:	Neurosensory Center Comprehensive Examination for Aphasia

[hard associates] (e.g., crush-dark). The entire list is repeated three times. A subject's score is equal to the total number of easy associations recalled across all three trials divided by two plus the total three trial score on the hard associates.

Raven Progressive Matrices:

The Raven Progressive Matrices is a culture-free test of general ability which correlates most highly with non-verbal tests (Hall, 1957; Urmer et al., 1960). It is also sensitive to reasoning and certain visuoperceptual disorders. The test consists of a number of nonrepresentational designs requiring visual pattern matching and analogy problem solving. It involves the conceptualization of spatial designs and numerical relationships which range from the very obvious to the very complex and abstract. Each test item consists of a pattern problem, similar to a puzzle, with one part removed. Under the problem puzzle are from six to eight pictured inserts, one of which correctly completes the puzzle. The subject then either points to the insert which corresponds to his choice or writes down the number of his choice on an answer sheet. The test is composed of five sets (Sets A through E) of 12 problems, each of which increases in level of difficulty as one moves from set to set. Subjects in this study were evaluated on Sets A through C. This decision was made because this is an untimed test and the usual time to completion of all sets may range up to an hour (Lezak, 1983). This was considered a prohibitive amount of time to devote to a single test in an extended battery. In addition, during the initial piloting of this study, several subjects refused to complete Sets D & E because of their difficulty level and, in fact, seemed to "ceiling out" towards the latter third of

Set C. It should be noted that normative data allowed for accurate estimations of complete test scores. Studies of the Raven's test-retest reliability range from .70 to .90 (Eichorn, 1975) with split-half reliability being reported as .67 (Dolke, 1976).

Test of Cerebral Dominance

Annett Handedness Questionnaire:

This 12-item questionnaire devised by Annett (1970) is used to classify individuals into one of six groups according to their pattern of manual preference: consistent right handers, inconsistent right handers, right ambidexters, left ambidexters, inconsistent left handers, and consistent left handers. Scoring is based on the number of "right" and "left" responses to primary and secondary questions of hand dominance, as assembled from association analyses (Annett, 1970). The procedure requires approximately five minutes to administer. It has been validated and shown by Lishman and McMeekan (1976) to have a test-retest reliability of .80 ($p < .01$).

Specific Cognitive Dimensions

Executive Processing

Initiation: Verbal Fluency Test (F,A,S)

Verbal fluency as measured by the F,A,S and similar tests has proven to be a sensitive indicator of cerebral dysfunction, particularly in the frontal lobe (Milner, 1967; Benton, 1968). The test consists of an examiner asking the subject to say as many different non-nominal words as he can think of which begin with the letter 'F' in sixty seconds. This procedure is then repeated for the letters 'A' and 'S'. The subject's score is the total number of acceptable words for all three letters produced within the alloted time limit. An individual's score is then adjusted for both age and education (years completed). The adjusted total score can then be expressed as a percentile.

Sequencing:

Trail Making Test (Parts A & B)

This test has been reported to be one of the most sensitive indicators of brain damage, particularly that involving the prefrontal regions (Reitan, 1958; Lewinsohn, 1973; Spreen & Benton, 1965). In Part A, the subject is asked to connect 25 consecutively numbered circles, while Part B requires the connection of 25 consecutively numbered and lettered circles with alternations between both sequences. In both parts, the examiner instructs the subject to connect the circles as quickly as he can. Total administration time for both parts is generally less than 10 minutes with age-adjusted norms providing percentile ranks being available (Davies, 1968). According to a review by Lezak (1983), the test-retest reliability coefficients for the two parts are .78 and .67 respectively.

Attention & Set:

Letter Cancellation Tests

Cancellation tasks are paper-and-pencil tests which require visual scanning, activation, and sustained attention. They generally follow the vigilance test pattern and consist of rows of letters interspersed with a designated target letter. The subject's task is to cross out all target letters as quickly as he can. Performance is scored for total errors as well as time to completion. While there are many versions of these tasks and adequate normative data is not available, cancellation tasks have found to be useful in a number of studies (Diller & Weinberg, 1977; Horne, 1973; Talland & Schwab, 1964; Talland, 1965; Weinberg & Diller, 1968) and shall be incorporated here in order to compare the performance of phenomenological subgroups.

Stroop Color-Word Test

The Stroop test measures a subject's ability to attend and to shift perceptual set as task demands change. The test consists of three sheets of standard letter size paper with each page having 100 items arranged in 5 columns of 20 items each. Golden (1978) describes his standardized version:

> Page 1 consists of the words "RED", Green", and "BLUE" arranged randomly and printed in black ink. No word is allowed to follow itself within a column. Page 2 consists of 100 items, all written as "XXX", printed in either red, green or blue ink. No color was allowed to follow itself within a column, nor to match the corresponding item on page 1. (For example, if the 13th item on page 1 was red, the 13th item on page 2 could not be printed in red ink). Page 3 consists of the words on page 1 printed in the colors of page 2. The two pages were blended item for item: Item 1 on page 1 is printed in the color of item 1 on page 2 to produce item 1 on page 3. In no case does the word and the color it is printed in match (pp. 3-4).

In administering the test, the subject is allowed 45 seconds in which to read as many items on each page as he can. Thus, total time of administration is approximately 2 minutes and 15 seconds, or 45 seconds per page. Errors are corrected by the examiner as they occur. The following three scores are generated: a word score (W) from Page 1, a color score (C) from Page 2, and a color-word score (C/W) from the total number of items read on Page 3. Cutoff scores suggesting cerebral dysfunction are W= < 75, C= ≤ 58, or CW = < 25. Measurement's of the reliability of Stroop scores have been consistent. Jensen (1965) reported reliabilities of .88, .79, and .71 for the three raw scores and Golden (1978) has reported reliabilities of .86, .82, and .73 respectively.

Categorical Set-Shifting:
Wisconsin Card Sorting Test

This test of category formation was designed to study the ability to shift mental set (Berg, 1948; Grant & Berg, 1948). Subjects may obtain a poor score on this task secondary to difficulty in maintaining set (Parsons, 1975), perserveratory errors (Drewe, 1974), and an inability to form concepts (Drewe, 1974) which would lead to difficulty in sorting by category. There is general agreement in the literature that this test is particularly sensitive to frontal lobe impairment (Drewe, 1974; Milner, 1963, 1964). Validation studies reported in the test manual indicate significant differentiation of brain damaged subjects from controls and significant correlation (r = .60) of total errors with the average impairment rating on the Halstead-Reitan Neuropsychological Battery. The test itself consists of 64 cards on which either a triangle, star, cross, or circle is printed in red, green, yellow, or blue. On each card, a given symbol is printed anywhere from one to four times. The subject's task is to place the cards, one at a time, under one of the four stimulus cards which include one red triangle, two green stars, three yellow crosses, and four blue circles. The subject sorts the cards according to a rule which he must deduce from the examiner's response following each placement. Whenever a subject places a card in a correct category, the examiner says "right". An incorrect placement elicits a "wrong" response from the examiner. Correct categories for placement begin with color, then form, shifting to number, returning again to color, etc. After ten consecutive placements in a correct category, the correct category shifts with the only notation made being that the examiner's response pattern changes suddenly from "right" to "wrong". The test concludes when the subject has made six runs of ten correct placements or has placed 128 cards without meeting criteria. Six scores are generated including the number of errors, correct responses, completed categories, perserverative repsonses, perserverative errors, and nonperserverative errors. Total time of administration is approximately 20 minutes.

Sensory-Motor Processing

Visual-Motor Speed & Coordination:

Purdue Pegboard Test

This motoric task has been found to be sensitive to the presence or absence of cerebral lesions (89% accuracy rate) as well as to the lateralization of lesions (Costa et al., 1963; Vaughan & Costa, 1962). Test-retest reliability coefficients have been reported to range from .60 to .76 per single trial increasing to between .82 and .91 when applying the Spearman-Brown prophesy formula for estimating the full test reliability (Tiffin, 1968). The test requires subjects to place pegs, one at a time, into a column of holes from top to bottom with their right hand, then their left hand, and finally with both hands simultaneously. This process is repeated for two trials and requires approximately 10 minutes to administer. It should be noted that there are two columns of holes side by side on the pegboard, the left side being used by the left hand with the right side being used by the right hand. The subject's score is the mean number of pegs correctly inserted under each of the three conditions within a 30 second time limit. Cut-off scores are available for individuals below and above 60 years of age (Vaughn & Costa, 1962).

Skilled Organized Movements:

Boston Apraxia Test

The Boston Apraxia test, adapted from the Parietal-lobe battery of the Boston Diagnostic Aphasia Examination (Goodglass & Kaplan, 1983), provides a brief (five minutes) assessment of ideomotor apraxia. The thirteen item test requires the subject to execute four different types of gestures upon command. The gestures include those having expressive and symbolic value, those which describe an object which is not present, those which have neither a symbolic nor semantic referent, and a question involving the execution of a simple four step serial command. The subject receives one point for each correct response.

Constructional Ability:

Stick Construction Test (BDAE)

The utilization of sticks to form geometric figures has long been included amongst informal clinical tests of constructional ability (Benton, 1967; Fogel, 1962; Goldstein & Scheerer, 1953; Hecaen & Assal, 1970). Materials for this test consist of 14 wooden sticks, seven of which are for examiner's demonstrations with the other seven being for the subject's reproductions. Each of the 14 standardized designs comprising the test is first assembled by the examiner who asks the subject to memorize it. After 10 seconds have elapsed, the examiner removes his sample and the subject is asked to reproduce the design. One point is earned for each correct reproduction up to a maximum score of 14 for the test. In order for credit to be awarded, each stick must be in the proper position. When a subject fails a given item, the examiner once again assembles it and the subject is given an opportunity too copy the item. The subject's ability to copy items is scored separately. The test yields two scores, that is, sticks to memory and sticks to copy. Normative data, in the form of means and standard deviations, are available by both age and education for both memory and copy conditions.

Somatosensory Processing:

Single & Double Simultaneous (Face-Hand) Stimulation Test

The SDSS is a simple test, requiring approximately 5 minutes to administer, which assesses specific somatosensory functioning by determing the accuracy with which subjects can identify single and double simultaneous tactile stimulation applied to cheek and/or hand. Stimuli are presented in a predetermined block of 20 listed on the SDSS score sheet. If there are no errors on the first trial, the findings are considered negative and the test is terminated. In order to document fluctuation in performance, a second trial is administered if the subject makes one or more errors on trial one. An error score of greater than three on trial one is considered evidence of "organic" cerebral dysfunction (Centofanti & Smith, 1979). The SDSS has been validated with patients having confirmed diagnoses of CVA disease or injury (N = 172) and with hospitalized psychiatric patients having various diagnoses (N = 10). Results of the assessment revealed that 56% of both of these groups earned abnormal SDSS scores as defined by >3 errors on the first trial. Interpretation of abnormal scores is such that if errors are generally restricted to the right or left hand and/or cheek, the results are considered evidence of a lateralized sensory deficit. When errors occur on both sides, results are considered to be evidence of a bilateral sensory deficit.

Linguistic Processing

Phonetic Processing:

Wepman Auditory Discrimination Test

The Wepman is included as a test of a subject's capacity to phonemically discriminate between similar sounding word-pairs (Wepman, 1958). The test requires a subject to tell whether both members of a word pair spoken by the examiner are the "same" or "different". There are a total of 40 word pairs with 30 pairs consisting of different but similar sounding words and the other 10 pairs consisting of the same word repeated twice. Total administration time required is approximately 5-7 minutes. The critical index is the number of failures to recognize subtle phonemic differences for which an error rate greater than 10% (>4 errors) is considered impaired (Wepman, 1958).

Lexical Processing:

Visual Confrontation Naming Test (BDAE)

This test is included in the protocol as a secondary measure of a subject's naming ability. The items on this test tend to be both culturally and educationally unbiased and it is felt that, since the items are less difficult than those on the Boston

Naming Test, the administration of both tests would yield a more reliable range of performance than the administration of the Boston Naming Test alone. The test takes approximately 5 minutes to complete and requires the subject to name objects, geometric forms, letters, actions, numbers, colors, and body parts pictured on two separate cards as the examiner points to them. When administering the body parts section of the test, the examiner points to the parts to be named on himself. Scoring is based on both response accuracy and latency. A maximum score of 114 is obtainable for the 38 items comprising the test. All paraphasias are copied and taiilied at the end. A perfect score (100% hit rate) is reportedly assumed for all normal subjects wth an internal reliability coefficient of .98 being noted (Goodglass & Kaplan, 1983). Both mean scores and standard deviations for aphasics are available in the manual for comparison.

Syntactic Processing:

Token Test (NCCEA)

This test is a very sensitive measure of the syntactic component of linguistic processing. It is quite simple to administer and to score. In general, all nonaphasic individuals with at least a 4th grade education can perform the task at a close to 100% level of accuracy. A total of twenty "tokens" in the shape of circles and rectangles colored in either red, green, yellow, blue, or white make up the test. The only requirement of the test is that the subject understand how to discriminate between circles and rectangles, between the colors of the tokens, and comprehend the verb and prepositions used in the instructions. Very few nonaphasic subjects fail to meet the above named requirements. Spreen and Benton's (1969) shortened version of this test consists of 39 oral commands given by the examiner to move the circles and rectangles in certain prearranged ways. The commands are arranged in five sections of increasing complexity. Failed items may be repeated once and the second score counted if the subject self-corrects. The subject earns one point for each correct response and thus, a total score of 39 is possible. Total time of administration is approximately 10 minutes.

Visual-Spatial Processing

Categorical Perception:

Hooper Visual Organization Test (VOT)

This test measures categorical perception and was originally developed to evaluate psychiatric patients for possible organic signs (Hooper, 1980). The VOT is an extremely helpful way to separate out the visual perceptual element from a subject's performance on the WAIS-R Object Assembly Test as well as other visuopractic tasks (Lezak, 1983). The test is made up of line drawings of 30 recognizable objects which have been cut into several pieces, in a manner similar to an "exploded" picture, with the subject's task being to name each object. A point is awarded for each correct response with intellectually intact subjects not making more than five incorrect responses. The VOT requires 10 minutes for completion and has a split-half reliability of .82 (Hooper, 1980).

Non-Categorized Perception:

Benton Facial Recognition Test

This test of noncategorical perception is particularly sensitive to posterior right hemisphere dysfunction (Benton & Van Allen, 1968, 1973; Tzavaras et al., 1971). The test, which requires about 15 minutes to administer, requires subjects to match identical front views of human faces, front with side views, and front views taken under different lighting conditions (Lezak, 1983). There are a total of 54 different matches with the range of possible scores between 25 to 54 since 25 of the photos can be identified by chance alone. The subjects' score is the total number of correct responses. Cut-off scores, defining different levels of impairment, indicate that a score of 39-40 raises the question of impairment with a score of 37-38 indicating impairment and any score less than 37 being consistent with severe impairment (Benton et al., 1983). Scores may also be expressed in terms of percentile ranks. This instrument's reliability, determined by large sample correlations between two forms, has been reported as .92 for brain damaged subjects, .88 for controls, and .93 for the combined sample (Benton et al., 1983).

Directional Orientation:

A Standardized Road Map Of Direction Sense

This test, requiring approximately 10 minutes for completion, was developed as a paper and pencil method of evaluating right-left directional orientation (Money et al., 1965). The test begins with a short demonstration trial during which the examiner traces a dotted pathway with a pencil. The subject's task is to name the direction taken at each turn, right or left. Following this demonstration trial, the examiner begins tracing the pathway on the actual test map. The map's broken line route is designed in such a way that there are four each of eight different possible types of turns (i.e., turning to the right after going away, back, right, & left) for a total of 32 turns. A subject's score is the total number of correct responses for a maximum score of 32. In a standardization study, Alexander and Money (1964) found that individuals over the age of 16 tend to level off at between two and three errors. This compares favorably with the mean of 1.92 errors found in another study which utilized a nursing student sample (Money, 1964). This same study also provides a mean number of errors for grades two through twelve.

Memory Processing

Verbal Memory:

Buschke Selective Reminding List Learning Test (Mixed List)

This verbal memory list learning test enables an examiner to differentially evaluate retention, storage, and retrieval by utilizing the method of selective reminding. The test consists of 10 noncategorized words which the examiner reads during the first trial. The subject must then recall as many of those words as he can. During each trial, the examiner repeats only those words which the subject has omitted during the immediately preceding trial with the subject then repeating all of the words which he can recall from the original list. The test continues in this manner until the subject either recalls the entire 10 word list for two consecutive trials or is unable to do so by the 10th trial. Normal control subjects are typically able to recall all ten words by the 3rd or 4th trials (Buschke & Fuld, 1974). The time required for this task varies according to the subject's ability but rarely exceeds 20 minutes. The test has been validated with victims of closed head injuries where total consistent retrieval scores discriminated significantly between patients with lesions in the left temporal, left non-temporal, and right hemisphere regions (Levin & Eisenberg, 1979).

Sentence Repetition Test (NCCEA)

The Sentence Repetition Test (Spreen & Benton, 1969) is included in this battery as a measure of a subject's short-term memory for syntactically related material. It is composed of twenty-two sentences of increasing length beginning with a single one syllable word and increasing to twenty words totaling twenty-six syllables. A subject's score is the total number of sentences recalled verbatim with a correction added for age and educational level.

Visual-Spatial Memory:

Benton Test Of Visual Retention [BVRT] (Admin. A) and BVRT Recognition Test

This test of visual-spatial memory has been demonstrated to be one of the more sensitive neuropsychological measures in distinguishing between subjects with cerebral brain damage from those with psychiatric disorders (Benton, 1974; Brillant & Gynther, 1963). In addition, it is particularly sensitive to impairments of the right hemisphere (Benton, 1974). Each of it's three equivalent forms is composed of 10 cards, eight of which have more than one design with most having three designs drawn in the horizontal plane. In most instances, the third figure is smaller than the other two and is drawn in either the left or right visual field. In Administration 'A', the one chosen for this study, the examiner exposes each card for 10 seconds with the subject's task being to draw the figure(s) which appeared on that card after the card is removed from sight. The subjects performance is scored for the number of correct reproductions as well as the total number of errors in accordance with test manual guidelines. Qualitative aspects of the errors are also noted (i.e. perserverations, omissions, rotations, distortions, etc.). Norms are arranged by age and intellectual capacity. The total correct and total error scores can be independently evaluated on a scale determined by the author to either "raise the question," or give a "strong indication" of acquired cognitive impairment. When Administration 'A' is employed, the time requirement of this test is approximately 15 minutes. The reliability coefficient for this particular administration has been reported as .85 under test-retest conditions (Benton, 1974; Benton et al, 1983). In order to assess memory without a motor component, the recognition form of the BVRT will also be administered. This task is similar to Administration 'A' of the BVRT in that ten designs are presented, one at a time, for a ten second period. However, rather than draw the design from memory, the subject must choose the correct stimulus design from amongst a four design multiple choice display. Thus, this task represents an assessment of recognition memory rather than on-line memory.

Cognitive Developmental Assessment

Given reports in the literature that schizophrenics with predominantly negative symptoms exhibit greater intellectual and premorbid deficiencies (Andreasen et al., 1982; Andreasen & Olsen 1982; Green & Walker, 1984) the possibility of preexisting developmental failures has been raised (Pogue-Geile & Harrow, 1984). Recently, several studies have provided evidence implicating early cognitive developmental deficits in negative subtype schizophrenics, as measured by Piagetian-type psychometric tests and educational levels (Kay et al., 1986a; Opler et al., 1984). These findings have underscored the importance of assessing the intellectual deficits of schizophrenics within a cognitive developmental framework in addition to more traditional neuropsychological methods. The Cognitive Diagnostic Battery (Kay, 1982) was chosen for inclusion into this study because it represents a well standardized instrument for assessing cognitive developmental issues. This battery, composed of five developmentally-based tests, was devised and standardized for use with psychiatric populations. Utilizing a Piagetian framework, the battery includes assessment of early conceptual maturation, higher order symbolic operations, egocentric versus socialized thinking, perceptual-motor development, temporal attention, psychomotor rate, and arousal-related (neuroleptic responsive) cognitive disruption [Table 6]. The subtests are brief, requiring only one to seven minutes each, are easily administered, demand little informational knowledge and, with the exception of the attention subtest, require little attention. The subtests have also been validated for repeated use (Kay, 1982). This assessment procedures has been geared to cognitive disorders seen in schizophrenia and provides a measurement of cognitive style (e.g., conceptual mode, etc.) rather than maximal ability in the manner of I.Q. and educational achievement tests. In addition, subtests of this battery have shown high reliability with schizophrenics, stability over time, sensitivity to treatment, concurrent and predictive validity, and validity for differentiating schizophrenics from other clinical and normal groups as well as for distinguishing among various schizophrenic subtypes including paranoid vs. hebephrenic vs. catatonic, acute vs. chronic, schizophreniform (atypical) vs. nuclear (typical), neuroleptic responders vs. neuroleptic nonresponders, and schizophrenics with a predominantly positive vs. negative symptom picture (Kay, 1982; Kay & Singh, 1979; Kay & Opler, 1985; Opler et al., 1984).

The individual subtests making up the Cognitive Diagnostic Battery are described below:

Color-Form Preference Test (CFP):

This is a 20-item similarity judgement test which evaluates conceptual maturity based on one's choice of hierarchical attributes for rendering classification (Kay, 1977, 1982; Kay & Singh, 1975). Patients are asked to match a standard card with one of three comparison cards, which may be done according to color, form, or neither cue. From an analysis of the response pattern, a measure of the emerging conceptual style and its prevalence is statistically derived using a chi square formulation. The result is then translated into one of the following four incremental stages of early cognitive development observed by Piaget (1952) and other experimental child psychologists (Bearison & Siegel, 1968; Kagan & Lemkin, 1961; Suchman & Trabasso, 1966): purposeless perserveration (up to one year of age), random response (age 2-3 years), classification by the salient attribute of color (age 4-6 years), or dominance by form (age 7-11 years). This procedure thus examines primitive bases for perceiving relationships as well as preconceptual modes of thinking. It's reliability coefficient, determined by split-half analysis, was found to be .91 for schizophrenics and .86 for normal subjects. A test-retest reliability index, obtained with schizophrenics over a one-week drug-free phase, was .82 (Kay, 1982).

Color-Form Representation Test (CFR):

An extension of the CFP, the CFR is a more advanced 20-item similarity judgement test which introduces the option of matching cards by figural representation (Kay, 1979). A standard card, depicting a key enclosed within a red circle, is matched to one of three comparision cards with vary in color, form, and pictorial content. The response pattern reflects conceptualization by use of more complex and symbolic clues, which by age 7 supercedes classification by color or form alone and is the maturer conceptual style which endures through adulthood (Bearison & Sigel, 1968). As such, this procedure indicates whether concept formation is guided by perceptually salient cues, as prevails prior to the emergence of abstract verbal language and cognitive operations (Piaget's stage of "intuitive thought"), or rather by cues which are semantically and symbolically more relevant (Piaget's stages of "concrete" and "formal operations") (Kay et al., 1975). The split-half reliability coefficient of the CFR when used with schizophrenics was found to be .94 with it's test-retest reliability index for this same group being .87 over a one week drug-free period (Kay, 1982).

Egocentricity of Thought Test (EOT):

The EOT, as a developmental measure of socialized thinking, derives from the Piagetian studies of how subject-object relations evolve in children (Piaget, 1952). Corresponding to the four sequential levels of cognitive development which succeed the sensorimotor stage, the four-level EOT depicts the four major phases in the acquisition of positional concepts: Preconceptual (<5 years of age), in which dependence on concrete operations precludes conceptualizing positional relations; egocentric (ages 5-8 years), characterized by subjective, self-centered operations whereby a child can identify right-left positions from his own perspective but not from another's; socialized (age 8-11 years), during which stage reversibility is first evidenced and right-left positions can be judged from one's own and another's standpoint but not in relation to a series of external objects; and objective (age 11 years to adult), corresponding to the stage of formal operations, whereby postional concepts are grasped independently of subjective and concrete referents (Kay & Singh, 1975). Test responses thus reflect whether thought and judgement are devoid of conceptual framework, subjectively anchored, socialized, or objective. The test-retest reliability among schizophrenics, over a one week drug-free period, was found to be .82 (Kay, 1982).

Progressive Figure Drawing Test (PFDT):

This procedure consists of copying seven simple designs (vertical line, circle, cross, square, triangle, tree, dimond) which children normally master at successive age periods between 2-6 years (Kay, 1980). Based on the developmental studies of Gesell (1924), Buhler (1935), and Terman and Merrill (1937), this subtest provides an index of perceptual-motor maturation and distinguishes developmental failure from subsequent cognitive abnormality in patients with combined developmental and psychiatric disorders. The reliability coefficient of the PFDT was found to be .93 by the split-half method and .96 by test-retest method following a 9-12 month interval (Kay, 1982).

Span of Attention Test:

The SOA provides a temporal measure of distractibility based on the mean length of time one sustains attention on a rote motor task, averaged over two trials (Kay & Singh, 1974). The test also yields a psychomotor rate, calculated as the ratio of items completed to time elapsed. The two scales are helpful in the assessment of attention deficit, hyperarousal, motor disturbance, and the neuroleptic response component of schizophrenic cognitive disorder (Kay & Singh, 1979). Test-retest reliability for schizophrenics, over a one week drug-free period, has been reported as .82 (Kay, 1982).

Table 6. **Overview of the Cognitive Diagnostic Battery**

Test	Area of Cognitive Assessment	Test Materials	Task Involved	Basis for Scoring	Contribution to the Battery	Time Requirement
CFP	Early conceptual development	20 sets of cards displaying combinations of color and form	Selecting optimal match to standard card on the basis of color, form, neither, or both cues	Response pattern analyzed for form dominance, color dominance, random response, perseveration, and detection of identical match	Assessment of conceptual style characteristic of pre-verbal and early verbal development, and an index of arousal-related cognitive dysfunction	3 - 6 minutes
CFR	Utilization of higher order concepts	20 sets of cards displaying combinations of color, form, and figural representation	Selecting optimal match to standard card on the basis of color, form, and/or representational cues	Number of optimal similarity judgments made	Assessment of verbal-symbolic stages of conceptual development and orientation to cues guided by semantic relevance vs. perceptual salience	3 - 6 minutes
EOT	Development of socialized thinking	A series of questions to determine whether thinking is preconceptual, socialized, or objective	To distinguish right and left laterabties from one's own viewpoint, the viewpoint of another, and relative to other objects	Scoring denotes the highest subtest level passed	Assessment of the later stages of subject object relations that bridge cognitive and social development, including evidence of egocentricity, subjectivity, reversibility, relativity, socialization, and objectivity of thought	1 - 3 minutes
PFDT	Perceptual motor development	7 cards displaying model drawings	Drawing designs by copy	Mental age associated with items passed	Assessment of level of perceptual motor development	1 - 3 minutes
SOA	Temporal attention and psychomotor pace.	Test sheet with 600 X's arranged in 26 rows	Encircling X's on the test sheet	Average number of seconds attending to task, and number of X's encircled per second	Assessment of typical span of concentration or distractibility and/of characteristic motor rate	1 - 7 minutes

(Kay, 1982)

Results

Organizational Format

The results of this study are presented in three main sections: Phenomenology, Neuropsychological Performance, and Performance on Cognitive Developmental Tests.

The section on positive/negative symptoms begins with analyses involving positive and negative assessments from both a dichotomous and dimensional perspective. Correlations of PANSS Scale scores with the SANS and SAPS are followed by an assessment of group differences on basic subject variables (i.e., age, education, neuroleptic dose, etc.). An evaluation of group differences in neuropsychological and cognitive developmental performance appears next. Following this, individual positive and negative symptoms are assessed with correlations within and between sets of positive and negative symptoms presented next. The results of the correlational analyses within and between sets of symptoms are then further analyzed in a principal components analysis. Since factors will concisely illustrate the "clustering" of symptoms found in correlational analyses, they will prove helpful in interpreting subsequent results. Next, correlations of individual symptoms with sample characteristics, measures of anxiety, neuropsychological test scores, and performance on cognitive developmental tasks will be presented.

The section on neuropsychological performance begins with a presentation of psychometric test results which describe the overall level of intellectual functioning of the entire sample as well as of positive and negative groups. Correlations between neuropsychological measures and subject variables are then shown.

The final section begins with an analysis of group performance on cognitive developmental tests from a dimensional perspective. The relationship of cognitive developmental test performance to sample characteristics, level of anxiety, and neuropsychological performance are then reviewed.

Positive and Negative Symptom Groups

Relationship of PANSS to other subtyping measures

In order to examine the relationship of PANSS Scale scores to scores on the SAPS (Andreasen, 1984) and SANS (Andreasen, 1983), two widely used rating instruments, Pearson correlations amongst these scales were obtained. As illustrated in Table 7, the PANSS Positive Scale correlated significantly with the SAPS (r = .62, df = 27, p < .001), the PANSS Negative Scale correlated significantly with the SANS (r = .60, df = 27, p < .001), and the PANSS Composite Scale (Positive summary score minus Negative summary score) correlated significantly with SAPS-SANS scores (r = .74, df = 27, p < .0001). An examination of cross-correlations revealed that the PANSS Positive Scale was not correlated with the SANS (r = .00) and the PANSS Negative Scale was not correlated with the SAPS (r = .01). Thus, these relationships appear to establish adequate criterion validity for the PANSS.

Group differences on subject variables

Patients were classified into positive and negative groups according to the criteria of Kay, Opler, and Fisbein (1987). Subject and course characteristics of positive and negative groups are shown in Table 8. Analyses conducted in

Table 7

Intercorrelaton of PANSS Scale Scores with SAPS and SANS Measures

PANSS Scale	SAPS	SANS	SAPS-SANS
Positive	.617***	.004	.433**
Negative	-.011	.600***	-.544***
Composite	.447**	-.477**	.743+
Gen. Psychopathology	-.164	.238	.371*

*P<.05; **P<.01; ***P<.001; +p<.0001, +df=27, one-tailed.

order to determine whether positive and negative groups were significantly different on any of these variables revealed no significant differences. However, when data were analyzed from a dimensional rather than dichotomous perspective, that is, the relative degree of positivity and negativity displayed by subjects (Table 9), a significant inverse relationship between age of onset and degree of positivity was noted (r = -.451, df = 28, p < .05, two tailed). No other significant relationships were noted during the

Table 8

Comparison of Positive and Negative Groups On Sample Characteristics

	Positive Groups		Negative Groups			
Control Var.	Mean	SD	Mean	SD	T	P[a]
Demographic Vars.						
Age	30.6	8.85	29.6	6.54	.34	NS
Years of Education	9.8	3.11	10.9	2.06	1.07	NS
Historical Vars.						
Age of Onset	20.8	6.03	21.9	4.14	.58	NS
Years of Illness	10.9	8.53	8.5	5.91	.90	NS
Treatment Vars.						
Days Hospitalized[b]	374.3	248.64	423.3	247.64	.52	NS
Neuroleptic Dose	785.3	513.05	1176.8	636.43	1.87	NS
Motor Control Scales:						
ERS	10.3	10.27	13.8	11.85	.88	NS
AIMS	4.0	6.40	2.2	2.61	.97	NS

continued

Table 8 (continued)

Comparison of Positive and Negative Groups On Sample Characteristics

Note.

[a]df = 28, two-tailed;

[b]Within past 18 mos.; df = 26

dimensional analysis. Thus, the hypothesis that a greater degree of negativity would be associated with an earlier age of onset, less education, a greater duration of illness, and a greater degree of motor abnormalities was not supported. While not directly hypothesized, a significant positive relationship was noted between neuroleptic dose and negativity. While the reason for this relationship is not entirely clear, two possibilities are that this may reflect either a greater degree of neuroleptic resistance on the part of patients displaying a predominance of negative symptoms or the negative syndrome may be, at least partially, neuroleptic exacerbated.

Table 9

Correlation of PANSS Scale Summary Scores With Subject Characteristics

Subject Characteristics	Pos.	Neg.	Composite	General Psychopath.
<u>Demographic Vars.</u>				
Age	.07	.15	.17	.00
Years of Education	-.16	.11	.21	.01
<u>Historical Vars.</u>				
Age of Onset	-.45*	- .29	-.09	-.43*
Years of Illness	.35	.00	.24	.26
<u>Treatment Vars.</u>				
Days Hospitalized[a]	.17	.37	-.17	.21
Neuroleptic Dose	-.03	.43*	.37*	.30
ERS	-.11	.30	-.32	.19
AIMS	-.02	.09	-.09	.18

*p<.05, df=28, two-tailed

[a]df=26

Group differences on neuropsychological variables

It was hypothesized that, while both groups would demonstrate cognitive impairment, subjects classified as negative would demonstrate a greater degree of neuropsychological impairment on tasks which tend to assess anterior functioning than subjects classified as positive.

An analysis of group performance on neuropsychological tasks revealed that verbal fluency yielded a significant differential performance by positive (mean = 38.6 $\pm$ 11) and negative (mean = 29.4 $\pm$12) groups (t = 2.12, df =26, p < .05). While verbal fluency was only one of six tests of anterior functioning included in the neuropsychological battery, it is noteworthy that it was the only test yielding a significant performance difference during dichotomous analysis.

Group differences on cognitive developmental tasks

It was hypothesized that negative group members would demonstrate less complete cognitive development than positive group members. As analysis of positive and negative group differences on cognitive developmental tasks failed to reveal any significant differences and, therefore, this hypothesis was not confirmed.

Individual Positive and Negative Symptoms

An analysis of individual symptoms on the PANSS was more revealing than that of dichotomous groups. Specifically, evidence was found suggesting that positive and negative symptoms, as defined in the literature by Andreasen (1982) and others (Kay & Opler, 1987a, 1987b) may be neither homogeneous within their own sets nor definitive of dichotomous subtypes. This evidence was found in correlational analyses within and between sets of pcsitive and negative symptoms as well as in the correlations of symptoms with other subtyping measures.

Consistency of Symptoms

Correlations within symptom sets

Given that the internal reliability of the PANSS has already been established with the coefficient alpha technique utilizing a large sample (N = 200; see page 41), interrelationships within symptom sets were examined to determine whether the constructs appeared to be unitary in this study. Intercorrelations within PANSS Positive subscale symptoms are presented in Table 10. Significant intercorrelations amongst PANSS Positive Scale symptoms were those between: (a) Delusions and the following:

conceptual disorganization ($r = .37$, $p < .05$), hallucinations ($r = .51$, $p < .01$) grandiosity ($r = .64$, $p < .01$) and suspiciousness ($r = .43$, $p < .05$); (b) Hallucinations and suspiciousness ($r = .38$, $p < .05$); (c) Excitement and hostility ($r = .55$, $p < .01$); (d) Suspiciousness and hostility ($r = .48$, $p < .01$). The highest intercorrelations of PANSS Positive Scale scores were those between: (a) Delusions and the following: hallucinations ($r = .51$, $p < .01$), and grandiosity ($r = .64$, $p < .001$); as well as (b) Excitement and hostility ($r = .55$, $p < .01$). All individual symptoms were significantly correlated with the PANSS Positive Scale summary score. General Psychopathology was found to be significantly correlated with the following positive symptoms: conceptual disorganization ($r = .73$, $p < .0001$), suspiciousness ($r = .55$, $p < .01$), and with the overall Positive Scale score ($r = .62$, $p < .001$).

A number of very significant intercorrelations were noted amongst symptom variables comprising the Negative Scale of the PANSS (Table 11). Significant intercorrelations found were those between : (a) Blunted affect and the following: emotional withdrawal ($r = .71$, $p < .0001$), poor rapport ($r = .60$, $p < .001$), passive/apathetic social withdrawal ($r = .68$, $p < .0001$), difficulty wth abstract thinking ($r = .39$,

Table 10

Intercorrelations of PANSS Positive Subscale and Summary Scores

	2	3	4	5	6	7	8	9
1. Delusions	.37*	.51**	.06	.64***	.43*	.15	.72+	.36
2. Conceptual Disorgan.		.31	.24	.21	.35	.31	.61***	.73+
3. Hallucina.			-.05	.20	.38*	.00	.54**	.36
4. Excitement				.20	.30	.55**	.49**	.19
5. Grandiosity					.32	.23	.65+	.25
6. Suspicious.						.48**	.68+	.55**
7. Hostility							.56**	.33
8. PANSS Pos. Scale Total								.62***
9. General Psychopath.								-

*p<.05, **p <.01, ***p<.001, +p <.0001, df=28, two-tailed

$p < .05$), and lack of spontaneity ($r = .73$, $p < .0001$); (b) Emotional withdrawal and the following: poor rapport ($r = .47$, $p < .01$), passive/apathetic social withdrawal

(r = .74, p < .0001), and lack of spontaneity (r = .70, p < .0001), (c) Poor rapport and the following: passive/apathetic social withdrawal (r = .56, p < .01) and lack of spontaneity (r = .67, p < .0001); (d) Passive/apathetic social withdrawal and the following: lack of spontaneity (r = .83, p < .0001) and stereotyped thinking (r = .41, p < .05); (e) Difficulty with abstract thinking and lack of spontaneity (r = .40 p < .05). All individual symptoms were significantly correlated with the PANSS Negative Scale summary score. General Psychopathology was found to be significantly correlated with the following negative symptoms: emotional withdrawal (r = .51, p < .0001), poor rapport (r = .47, p < .01), passive/apathetic social withdrawal (r = .59, p < .001), lack of spontaneity (r = .51, p < .01), stereotyped thinking (r = .70, p < .0001), and with the overall Negative Scale score (r = .71, p < .0001).

<u>Group differences between symptom sets</u>

When mean ratings by positive and negative group members on criterion symptoms of the PANSS were analyzed, neither group differed significantly from the other across all individual symptoms specific to a particular group thus mitigating against the homogeneity of sets of positive and negative symptoms (Table 12). Within the positive symptom

Table 11

Intercorrelation of PANSS Negative Subscale Scores and Summary Scores

	2	3	4	5	6	7	8	9
1. B.A	.71^{+}	.60***	.68^{+}	.39*	.73^{+}	.15	.79^{+}	.34
2. E.W.		.47**	.74*	.33	.70^{+}	.32	.81^{+}	.65^{+}
3. P.R.			.56**	.31	.67^{+}	.30	.71^{+}	.47**
4. P.A.-S.W.				.34	.83^{+}	.41*	.87^{+}	.59***
5. D.A.T.					.40*	.10	.51	.30
6. L.O.S.						.29	.88^{+}	.51**
7. S.T.							.48**	.70^{+}
8. Neg Total								.71^{+}
9. Gen. Psy.								-

<u>Note.</u>

B.A. - Blunted affect

E.W. - Emotional withdrawal

P.R. - Poor rapport

P.A. - Passive/Apathetic social withdrawal

D.A. - Difficulty with abstract thinking

continued

Table 11 (continued)

Intercorrelation of PANSS Negative Subscale Scores and Summary Scores

Note. (continued)

L.S. - Lack of spontaneity and flow of conversation

S.T. - Stereotyped thinking

N.S. - PANSS Negative Scale summary score

*p <.05, **p<.01, ***p <.001, +p<.0001, df= 28, two-tailed

cluster, positive and negative subjects differed significantly on only one symptom, hallucinatory behavior (t = 2.17, df = 28, p <.05). The negative symptom cluster proved to be a better discriminator of positive and negative subjects with scores on five of seven symptoms being significantly different (blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, and lack of spontaneity).

Comparison of Positive and Negative Subgroups on PANSS summary score and PANSS Factors

While, as expected, positive and negative group members obtained PANSS Positive and Negative Scale summary scores which were significantly different, the two groups did not differ from one another in terms of general psychopathology ($p = .26$). When the relationship between group membership and PANSS factors (see page 104) was analyzed, significant differences were noted on only two of three factors. As expected, positive and negative group membership were positively associated with the "core" positive symptoms factor (Factor 3, $t = 2.49$, df = 28, $p < .02$) as well as to the "core" negative symptoms factor (Factor 1, $t = 4.58$, df = 28, $p = .0001$) respectively. The two groups did not, however, differ significantly on the excitable/cognitive factor (Factor 3, $t = .706$, $p = .49$). Thus, it seems that this sample is better conceptualized in terms of a Venn Diagram in which positive and negative groups differ significantly on Factors 1 and 3 while sharing traits included within Factor 2.

Correlations between symptom sets

Correlations within positive and negative symptom sets demonstrated that neither set was homogenous. Furthermore, since the PANSS Positive-Negative Scale summary score correlation was not negative, the hypothesis that such symptoms define opposite ends of a continuum (Andreasen & Olsen, 1982) was not supported. The intercorrelations between PANSS Positive and Negative Subscale symptoms is displayed in

Table 12

Comparison on Mean Ratings by Positive and Negative Subjects on Criterion Symptoms of the PANSS

	Schizophrenic Subtype					
	Positive		Negative			
Criterion Sx	Mean	SD	Mean	SD	T	P
<u>Positive Cluster:</u>						
Delusions	3.91	1.24	2.89	1.67	1.90	.07
Conceptual Disorganization	3.93	1.60	3.56	1.22	0.71	.48
Hallucinatory behavior	3.37	1.63	2.21	1.25	2.17	.04
Excitement	2.84	1.71	1.82	.91	2.00	.06
Grandiosity	3.57	1.50	2.66	1.65	1.60	.12
Suspiciousness	3.20	1.22	3.09	.62	.32	.75
Hostility	2.22	1.47	1.95	0.74	0.63	.54
<u>Negative Cluster:</u>						
Blunted Affect	2.12	1.02	3.85	0.67	5.40	.0001
Emotional withdrawal	2.23	1.25	3.86	0.77	4.00	.0004

Table 12 (continued)

Comparison of Mean Ratings by Positive and Negative Subjects on Criterion Symptoms of the PANSS

	Schizophrenic Subtype					
	Positive		Negative			
Criterion Sx	Mean	SD	Mean	SD	T	P
Negative Cluster						
Poor rapport	1.77	.78	2.66	0.92	2.88	.008
Passive/apathetic social w/drawal	1.66	1.42	3.53	1.62	3.38	.002
Difficulty with abstract thinking	3.69	1.02	4.29	1.07	1.57	.13
Lack of Spontaneity & Flow of conver.	1.80	1.21	3.69	1.40	4.00	.0004
Stereotyped thinking	2.87	1.31	2.92	1.27	0.11	.91

df=28, two-tailed

Table 13. There were only two significant negative correlations: excitement and blunted affect (r = .45, p < .05) as well as excitement and difficulty with abstract thinking (r = -.39, p < .05). Only blunted affect appeared to have a consistent pattern of negative correlations with the PANSS Positive Scale symptoms. The PANSS Positive Scale score was not significantly correlated with the PANSS Negative Scale score (r = .13, p > .10). Thus, while positive and negative scales may not represent two homogenous subgroups, it is apparent that they are not mutually exclusive and that differences between the groups of symptoms do in fact exist.

In examining summary scores more closely, it was found that the PANSS Positive Scale score was positively correlated to stereotyped thinking (r = .48, p <.01) and the PANSS Negative Scale score was positively correlated to conceptual disorganization (r = .42, p < .05). The results of a principal components analysis of the fourteen clinical variables from the PANSS Positive and Negative Scales as shown in Table 14. The initial solution produced three principal components with Eigenvalues greater than 1.0 which together accounted for 66% of the variance. The rotated (Varimax) factor pattern is also shown in Table 14.

Table 13
Intercorrelation of Positive and Negative Symptom Measures

	B.A	E.W.	P.R.	P/A	D.A.T	L.S	S.T.	N.S.
Delusions	-.13	.05	.07	.19	.05	.07	.33	.13
Conceptual Disorgan.	.19	.38*	.32	.30	.11	.26	.72**	.42*
Hallucinations	-.13	.07	-.00	.17	.14	.03	.18	.10
Excitement	-.45*	-.22	-.14	-.23	-.39*	-.29	.26	.27
Grandiosity	-.27	-.02	.05	-.04	-.10	-.01	.08	.06
Suspiciousness	-.22	.05	.27	.14	.07	.18	.43*	.17
Hostility	-.19	-.04	-.01	-.09	-.25	-.02	.33	.04
PANSS Positive	-.27	.06	.12	.08	-.07	.04	.48**	.13

Note.

B.A. - Blunted affect

E.W. - Emotional withdrawal

P.R. - Poor rapport

P.A - Passive/apathetic social withdrawal

continued

Table 13 (continued)

Intercorrelation of Positive and Negative Symptom Measures

D.A. - Difficulty with abstract thinkng;

L.S - Lack of spontaneity & flow of conversation

Note. (continued)

S.T. - Stereotyped thinking

N.S. - Panss Negative Scale summary score

*$p<.05$, **$p<.01$, ***$p<.0001$, df =28, two tailed

The first factor, with high loadings on blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty with abstract thinking, and lack of spontaneity, appears to represent core negative symptoms common to both Positive and Negative Scales. Factor 2 appears to represent a general (i.e., common to both positive and negative subscales) excitable/cognitive factor. The third factor, with high loadings on delusions, hallucinatory behavior, grandiosity, and suspiciousness, appears to reflect core positive symptoms.

Table 14

Principal Components Analysis of Positive and Negative Symptoms

	EV[a]	Pr[b]	Cum[c]
Initial Solution			
Factor 1	4.42	.316	.471
Factor 2	3.22	.230	.266
Factor 3	1.58	.113	.262

Rotated Factor Pattern[1]

	Factor		
Variable	1	2	3
Delusions	.06	.11	**.88**
Conceptual Disorganization	.43	**.55**	.37
Hallucinatory Behavior	.06	.08	**.76**
Excitement	.33	**.79**	.01
Grandiosity	.12	.18	**.67**
Suspiciousness	.12	.52	**.55**
Hostility	.09	**.81**	.67
Blunted Affect	**.86**	.20	.27
Emotional Withdrawal	**.84**	.03	.00
Poor Rapport	**.75**	.11	.04
Passive/Apathetic Social W/drawal	**.87**	.01	.12

Table 14 (continued)

Principal Components Analysis of Positive and Negative Symptoms

Variable (continued)	1	2	3
Difficulty with Abstract Thinking	**.50**	.37	.19
Lack of Spontaneity & Flow of Conversation	**.89**	.01	.03
Stereotyped Thinking	.44	**.61**	.26

Note.

1 Rotation method was Varimax

a Eigenvalue

b Proportion of variance explained

c Cumulative proportion of variance accounted for

Relationship of PANSS Positive and Negative Summary Scores to PANSS Factors

The results of a correlation analysis of the relationship of PANSS factors to PANSS Positive and Negative Scale summary scores are listed in Table 15. As expected, "core" negative symptoms (PANSS Factor 1) was significantly associated with the PANSS Negative Scale summary score

(PANSS Factor 2) and "core" positive symptoms (PANSS Factor 3) were related to the PANSS Positive Scale summary score ($r = .96$, $p < .0001$ and $r = .75$, $p < .0001$ respectively). The significant relationship between the excitable/cognitive factor and the PANSS Positive Scale summary score ($r = .58$, $p < .001$) may be attributable to the fact that three out of the four symptoms comprising this factor are Positive Scale symptoms. In addition, it should be noted that the Positive Scale was not significantly related to the "Core" Negative

Table 15

PANSS Positive and Negative Scale Summary Score Correlates of PANSS Factors

	PANSS Subscale Summary Scores	
	Positive	Negative
"Core" Negative Symptoms	.02	.96**
Excitable/Cognitive	.58*	.04
"Core" Positive Symptoms	.75**	.07

*$p < .001$, **$p < .0001$, df=28, two-tailed.

Symptoms factor (*r* = .02, *p* > .10) nor was the Negative Scale related to either the excitable/cognitive factor (*r* = .04, *p* > .10) or the "core" positive symptom factor (*r* = .07, *p* >.10).

Correlation of PANSS Subscale Symptoms and PANSS Factors With Subject Characteristics

The correlations between PANSS Positive Scale symptom measures and subject characteristics are shown in Table 16. Age of onset was found to be negatively correlated with each of the following PANSS Positive Subscale symptoms: conceptual disorganization (*r* = -.47, df = 28, *p* < .01), hallucinatory behavior (*r* = -.42, df = 28, *p* < .05), and suspiciousness (*r* = -.55, df = 28, *p* < .01). Two subject variables yeilding positive correlations were years of illness and hallucinatory behavior (*r* = .38, df = 28, *p* < .05) as well as days hospitalized and delusions (*r* = .40, df = 26, *p* < .05). All other correlations between the symptom measures and age, education, age of onset, years of illness, days hospitalized, neuroleptic dose, and motor abnormalities were nonsignificant.

When subject variable correlates of PANSS Negative Subscale symptoms were examined, neuroleptic dose was found to be significantly correlated with blunted affect ($r = .42$, $p < .05$), emotional withdrawal ($r = .43$, $p < .02$), poor rapport ($r = .49$, $p < .01$), and with the PANSS Negative Scale summary score ($r = .43$, $p < .05$). Both days hospitalized and extrapyramidal signs were associated with passive/apathetic social withdrawal ($r = .45$, $p < .05$ and $r = .57$, $p < .001$ respectively). A significant inverse relationship was noted between age of onset and stereotyped thinking ($r = -.44$, $p < .05$).

When the relationship of PANSS Factors to subject characteristics were examined, "core" negative symptoms (PANSS Factor 1) were found to be significantly related to neuroleptic dose ($r = .44$, df = 28, $p < .05$). This is similar to the finding, during dimensional analysis, that the PANSS Negative Scale summary score was related to neuroleptic dose ($r = .43$, $p < .05$). The excitable/cognitive factor (PANSS Factor 2) was not associated with any of the subject characteristics. "Core" positive symptoms (PANSS Factor 3) were related to an earlier age of onset ($r = -.48$, df = 28, $p < .01$) and to length of hospitalization ($r = .38$, df = 28, $p < .05$). While the PANSS Positive Scale summary score was inversely related to age of onset during dimensional analyses ($r = -.45$, $p < .05$), it was not found to be associated with days hospitalized.

Table 16

Significant Subject Characteristics Correlates of PANSS Positive Subscale Symptom

Positive Scale Symptom:	r
Delusions	
Days Hospitalized	.40*
Conceptual Disorganization	
Age of Onset	.47**
Hallucinatory Behavior	
Age of Onset	-.42*
Years of Illness	.38*
Excitement	NS
Grandiosity	NS
Suspiciousness	
Age of onset	-.55**
Hostility	NS
Positive Scale Total	
Age of Onset	-.45*

*$p<.05$, **$p<.01$., df=28, two-tailed.

Affect

Group differences on Manifest Affect Rating Scale (MARS) Factors

An assessment of affect was included in the clincial evaluation of subjects because impaired affect has been considered one of the hallmarks of the "defect state" in schizophrenia (Feighner et al., 1972). When the effect of positive or negative group membership on MARS factors (Alpert & Rush, 1983) was assessed, significant group differences were found on all three factors. Specifically, the negative group displayed a greater degree of emotional unrelatedness (MARS factor 1) ($t = 3.75$, df = 28, $p < .0008$, two tailed) and expressive immobility (MARS factor 2) ($t = 2.12$, df = 28, $p < .05$, two tailed). The positive group, on the other hand, displayed a greater degree of inappropriatness of affect (MARS factor 3) ($t = 2.22$, df = 28, $p < .05$, two tailed).

Correlation of Manifest Affect Rating Scale (MARS) Factor scores with the Positive and Negative Syndrome Scale (PANSS)

The relationship of MARS factor scores to scores on the PANSS was investigated using a correlational anaysis (Table 18). Emotional unrelatedness (MARS Factor 1) was found to be inversely associated with only one PANSS positive symptom excitement ($r = -.41$, df = 28, $p < .05$). It was however, positively related to six of the seven PANSS negative symptoms and to the PANSS Negative Scale summary score. Specifically, it was related to blunted affect ($r = .78$, df = 28, $p < .0001$), emotional withdrawal ($r = .68$, df = 28, $p < .0001$), poor rapport ($r = .51$, df = 28, $p < .01$),

Table 17

Significant Subject Characteristics Correlates of PANSS Negative Subscale Symptoms

Negative Subscale Symptom:	r
Blunted Affect	
Neuroleptic Dose	.42*
Emotional Withdrawal	
Neuroleptic Dose	.43*
Poor Rapport	
Neuroleptic Dose	.49**
Passive/Apathetic Social Withdrawal	
Extrapyramidal Scale	.57***
Days Hospitalized	.45*
Difficulty with Abstract Thinking	NS
Lack of Spontaneity & Flow of Conversation	NS

Table 17 (continued)

Significant Subject Characteristic Correlates of PANSS Negative Subscale Symptoms

<u>Negative Subscale Symptom (con't)</u>	<u>r</u>
<u>Stereotyped Thinking</u>	
Age of Onset	-.44*
<u>Negative Scale Total</u>	
Neuroleptic Dose	.43*

*p <.05, **p<.01, ***p<.001, df=28, two-tailed.

passive/apathetic social withdrawal (r = -.65, df = 28, p < .0001), difficulty with abstract thinking (r = -.37, df = 28, p < .05), lack of spontaneity and flow of conversation (r = .66, df = 28, p < .0001), and with the PANSS Negative Scale summary score (r = .70, df = 28, p <.0001). It was also related to general psychopathology (r = .38, df = 28, p < .05). Expressive immobility (MARS factor 2) was only related to PANSS negative symptoms. It was significantly associated with blunted affect (r = .39, df = 28, p < .05), emotional withdrawal (r = .42, df = 28, p < .05), poor rapport (r = .39, df = 29, p < .05), passive/apathetic social withdrawal (r = .54, df = 28, p < .01), difficulty with abstract thinking

(r = .54, df = 28, p < .01), lack of spontaneity and flow of conversation (r = .54, df = 28, p < .01), and with the PANSS Negative Scale summary score (r = .56, df = 28, p < .01). As was the case with emotional unrelatedness (MARS Factor 1), expressive immobility (MARS Factor 2) was also associated with general psychopathology (r = -.42, df = 28, p < .02). Contrary to this, inappropriateness of affect (MARS Factor 3) was only related to one PANSS positive symptom, excitement (r = .40, df = 28, p < .05) and the PANSS Positive Scale summary score (r = .40, p < .05). This factor was additionally found to be inversely associated with one PANSS negative symptom, blunted affect (r = -.41, p < .05). It was not significantly associated with either PANSS Negative Scale summary score nor with general psychopathology.

Table 18

Significant Positive and Negative Syndrome Scale Correlates of Manifest Affect Rating Scale (MARS) Factors

MARS Factor	r
1 (Emotional Unrelatedness)	
Excitement	-.41*
Blunted affect	.78***
Emotional withdrawal	.68***
Poor rapport	.51**
Passive/apathetic social withdrawal	.65***
Difficulty with abstract thinking	.37*
Lack of spontaneity & flow of conversation	.66***
PANSS Negative Scale summary score	.70***
General Psychopathology Scale summary score	.38*
2 (Expressive Immobility)	
Blunted affect	.39*
Emotional withdrawal	.42*
Poor rapport	.39*
Passive/apathetic social withdrawal	.54**
Difficulty with abstract thinking	.54**
Lack of spontaneity & flow of conversation	.56**

continued

Table 18 (continued)

Significant Positive and Negative Syndrome Scale Correlates of Manifest Affect Rating Scale (MARS) Factors

MARS Factor	r
2 (Expressive Immobility) (continued)	
PANSS Negative Scale summary score..........................	.56**
General Psychopathology Scale summary score.......	.42*
3 (Inappropriateness of Affect)	
Excitement..	.40*
Blunted affect..	-.41*
PANSS Positive Scale summary score..........................	.40*

*p<.05, **p<.01, ***p<.0001, df=28, two-tailed

Correlations of symptoms with neuropsychological findings

Correlations were performed between each of the neuropsychological test variables and each of the symptoms comparing the PANSS Positive and Negative Scales. Those correlations significant either at or better than the .05 significance level (two-tailed) are presented in Tables 19 and 20.

The significant neuropsychological test correlates of the positive symptom measures are shown in Table 19. Of the positive symptoms, conceptual disorganization was associated with poor performance on tests of general intellectual capacity, memory, and executive functioning. Hallucinatory Behavior was associated with poor motoric functioning, specifically, that of fine motor speed and coordination. Excitement seemed related to a decrement in psychomotor processing requiring attention. Finally, hostility was related to visual-spatial processing.

A different pattern of neuropsychological test results was significantly correlated with both negative symptoms and the negative summary score as well (see Table 20). Specifically, six of seven symptoms in the PANSS Negative Scale (blunted affect, emotional withdrawal, passive/apathetic social withdrawal, difficulty with abstract thinking, lack of spontaneity and flow of conversation, and stereotyped thinking) were related to impaired performance on at least one task associated with anterior dysfunction. As an example, five of seven symptoms were associated with poor performance during an evaluation of verbal fluency. In examining the negative symptoms

Table 19

Significant Neuropsychological Test Correlates of PANSS Positive Subscale Symptoms

Symptom	r
Delusions	
Benton Visual Retention Test (Recognition)	.42*
Conceptual Disorganization	
MQ (WMS)	-.43*
Paired Associate Learning (WMS)	-.42*
WCST Perserverative Errors	.43*
WCST Categories Achieved	-.41*
Full Scale IQ (WAIS-R)	-.53**
Verbal IQ (WAIS-R)	-.52**
Performance IQ (WAIS-R)	-.44*
Hallucinatory Behavior	
Purdue Pegboard (Left Hand)	-.49*
Purdue Pegboard (Right Hand)	-.49**
Purdue Pegboard (Bimanual)	-.40*
Excitement	
Stick Test	-.44*
Letter Cancellation (H) Time	-.40*
Boston Apraxia	-.38*

continued

Table 19 (continued)

Significant Neuropsychological Test Correlates of PANSS Positive Subscale Symptoms

Symptom	r
Grandiosity	NS
Suspiciousness	NS
Hostility	
Ravens Progressive Matrices	-.43*
Stick Test	-.44*
Positive Scale Score	
Purdue Pegboard (Right Hand)	-.40*

Note.

WMS = Wechsler Memory Scale; WCST = Wisconsin Card Sorting Test; WAIS-R = Wechsler Adult Intelligence Scale-Revised; CDB = Cognitive Diagnostic Battery

*$p<.05$, **$p<.01$, two-tailed (See appendix for individual neuropsychological test degrees of freedom).

individually, blunted affect was associated with poor verbal performance (Verbal Fluency Test and Verbal IQ). While emotional withdrawal was also associated with the same pattern of verbal performance, it was additionally associated with a lower Full Scale IQ. Poor rapport was

Table 20

Significant Neuropsychological Test Correlates of PANSS Negative Subscale Symptoms

Symptom	r
Blunted Affect	
Verbal Fluency	-.56**
Verbal IQ (WAIS-R)	-.42*
Emotional Withdrawal	
Verbal Fluency	-.49**
Full Scale IQ (WAIS-R)	-.37*
Verbal IQ (WAIS-R)	-.40*
Poor Rapport	
Wepman Auditory Discrimination Test	-.45*
Passive-Apathetic Social Withdrawal	
Verbal Fluency	-.46**
Purdue Pegboard (left hand)	-.58***
Difficulty with Abstract Thinking	
Verbal Fluency	-.41*
Full Scale IQ (WAIS-R)	-.38*

continued

Table 20 (continued)

Significant Neuropsychological Test Correlates of PANSS Negative Subscale Symptoms

Symptom	r
Lack of Spontaniety & Flow of Conversation	
Verbal Fluency	-.43*
Purdue Pegboard (right hand)	-.42*
Stereotyped Thinking	
MQ (WMS)	-.43*
Paired Associate Learning (WMS)	-.54**
WCST Persererative Errors	.44*
WCST Categories Achieved	-.42*
Full Scale IQ (WAIS-R)	-.38*
Performance IQ (WAIS-R)	-.37
Negative Scale Total	
Full Scale IQ (WAIS-R)	-.38*
Verbal IQ (WAIS-R)	-.33*
Verbal Fluency	-.45*
Purdue Pegboard (Left Hand)	-.41*
Purdue Pegboard (Right Hand)	-.40*

continued

Table 20 (continued)

Significant Neuropsychological Test Correlates of PANSS Negative Subscale Symptoms

Note.

WMS = Wechsler Memory Scale; WCST = Wisconsin Card Sorting Test; WAIS-R = Wechsler Adult Intelligence Scale-Revised.

$^{*}p<.05$, $^{**}p<.01$, $^{***}p<.001$, two-tailed (See appendix for individual neuropsychological test degrees of freedom).

related to difficulty with auditory discrimination. Passive/apathetic social withdrawal and lack of spontaneity and flow of conversation were both associated with poor performances on the verbal fluency and the Purdue Pegboard. It should be noted, however, that a difference in lateralized performance on the Purdue was apparent. Specifically, on the Purdue Pegboard, these symptoms were related to poor left and right handed performance respectively. In addition to being associated with an impairment of verbal fluency, difficulty with abstract thinking was also related to an overall lowering of Full Scale IQ. Of all the Negative Scale symptoms, stereotyped thinking was associated with a poor performance on the greatest number of neuropsychological variables. Specifically, it was assoicated with a poor performance on tests of verbal and visual-spacial memory (WMS MQ, Paired Associate Learning [WMS], and BVRT), general intellectual capacity (Full Scale IQ), and executive functioning (WCST- perserverative errors and categories achieved).

The hypothesized greater degree of anterior dysfunction amongst negative versus positive syndrome subjects was supported to the extent that a greater number of negative symptoms were associated with anterior dysfunction than was the case with positive symptoms.

Neuropsychological Performance

Level of neuropsychological functioning

It was hypothesized that all subjects, both positive and negative would demonstrate some degree of cognitive impairment whether viewed from a dichotomous or dimensional perspective. The sample's performance on widely used tests of cognitive integrity as well as on instruments used for the prediction of brain damage is depicted in Tables 21and 22.

Table 21

General Indices of Cognitive Integrity

Intelligence Test Results For Sample

Wechsler Adult Intelligence Scale-Revised

Verbal Subtests	ACSS[a] Mean	ACSS[a] SD	Performance Subtests	ACSS[a] Mean	ACSS[a] SD
Information	7.2	2.7	Picture Completion	6.0	2.5
Digit Span	7.1	2.6	Picture Arrange.	5.6	2.4
Arithmetic	6.5	2.6	Block Design	6.6	2.7
Vocabulary	6.9	2.6	Object Assembly	6.4	2.5
Comprehension	6.2	2.4	Digit Symbol	5.0	1.4
Similarities	7.2	2.5			

	Mean	SD	Range
Verbal IQ	82.1	11.2	56-110
Performance IQ	74.9	10.7	56-97
Full Scale IQ	77.6	10.1	53-100

Raven's Progressive Matrices (Standard)

	Mean	SD	Range
Total Score[b]	20.8	7.0	29-35

Median Percentile Score[c] = 10th

continued

Table 21 (continued)

General Indices of Cognitive Integrity

Wechsler Memory Scale

Subtest	Mean	SD
Information	4.9	1.3
Orientation	4.9	0.7
Mental Control	5.2	2.4
Memory for Passages	6.2	3.6
Digits Total	9.9	2.1
Visual Reproduction	7.1	4.0
Paired Associate Learning	10.0	4.6
MQ	80.3	18.6

NOTE

[a] ACSS = Age Corrected Scaled Score (N=30)

[b] Sets A,B,C

[c] Interpolated

Performance on the WAIS-R, Raven's Progressive Matrices, and Wechsler Memory Scale is shown in Table 21. The mean

WAIS-R Full Scale IQ of the patients (77.6) was within the borderling range of intellectual ability (Wechsler, 1981), a range not untypical for the schizophrenic population (Kay, 1979; Payne, 1973). Six subjects had Full Scale IQ scores which were within the range of mild mental retardation (See Appendix 1 for the IQ Scores of each subject). Raven's Progressive Matrices total interpolated score indicated that the sample's performance exceeded that of only 10% of the population (See Table 22).

On tests widely used as "screening" instruments for the identification of brain damage, from 22-85% of the sample was classified as brain damaged according to standard cutoff scores (see Table 22).

Relationship of neuropsychological variables to PANSS Scale Factors

A correlational analysis was conducted in order to examine significant relationships between neuropsychological variables and PANSS factors. Results, presented in Table 23, indicate that "core" negative symptoms (PANSS Factor 1) were inversely related to performance on the Full Scale and Verbal IQ Scales of the WAIS-R (r = -.42, p < .05 and r = -.43, p < .05 respectively) as well as to verbal fluency (r = -.58, p < .01). The

Table 22

Classification of Patients by Instruments Used to Predict "Brain Damage"

		Number Scoring		
		Below	Above	
Instrument	Score	Cutoff	Cutoff	"B.D."
Purdue Pegboard[a]				
Preferred	<26	09	18	33%
Nonpreferred	<22	06	22	23%
Bimanual	<18	06	21	22%
Trail-Making Test[b]				
Part A	>40s	22	07	76%
Part B	>92s	23	04	85%
Benton Visual Retention Test[c]				
Number Correct	≥-3	15	14	52%
Number Errors	≥+4	21	08	72%

continued

Table 22 (continued)

Classification of Patients by Instruments Used to Predict "Brain Damage"

Note.

[a] Scores are number of pegs placed in two 30-seconds trials (Smith & Goldberg, 1979).

[b] Time to Completion (Reitan, 1964).

[c] Cutoff scores are those which either suggest or provide a strong indication of acquired cognitive impairment (Benton, 1974).

excitable/cognitive factor (PANSS Factor 2) was inversely related to performance on a verbal memory task, paired associate learning ($r = -.39$, $p < .05$). it was also related to poorer performances on a constructional (Stick test: $r = -.43$, $p < .05$). Finally, the third PANSS factor, "core" positive symptoms, was found to be inversely related to right-handed performance on the Purdue Pegboard test.

Correlations of neuropsychological measures with subject characteristics.

Correlations of each of the neuropsychological measures with age, education, age of onset, years of illness, days of hospitalization, chlorpromazine equivalence, and motor

Table 23

Significant Neuropsychological Variable Correlates of PANSS Factors

Factor	r
"Core" Negative Symptoms	
Full Scale IQ (WAIS-R)	-.42*
Verbal IQ (WAIS-R)	-.43*
Verbal Fluency	-.58**
Excitable/Cognitive	
Paired Associate Learning (WMS)	-.39*
Stick Test	-.43*
Letter Cancellation Test (Time to completion)	.40*
"Core" Positive Symptoms	
Purdue Pegboard (Right hand)	-.40*

*p <.05, **p <.01, two-tailed. (See appendix for individual neuropsychological test degrees of freedom).

sample characteristics (Extrapyramidal Rating Scale and the Abnormal Involuntary Movement Scale) are shown known Table 24.

It was hypothesized that the general intellectual capacity of subjects would be positively correlated to age of onset and educational attainment. Age of onset was found to be significantly correlated with both the Full Scale ($r = .37$, df = 28, $p < .05$) and Performance IQ's ($r = .54$, df = 28, $p < .01$) of the WAIS-R. Educational attainment was related to all three WAIS-R summary scores: Full Scale IQ ($r = .59$, df = 28, $p < .001$), Verbal IQ ($r = .61$, df = 28, $p < .001$), and Performance IQ ($r = .47$, df = 28, $p < .01$). Thus, while verbal skills seem related only to educational level, overall general intellectual capacity does seem related to both of these sample characteristics.

Although not specifically hypothesized, there were predictable relationships of educational attainment and a number of neuropsychological test variables dealing with general intellectual capacity, executive functioning, visual-spatial processing, and memory (both verbal and visual-spatial). Also not hypothesized was a significant inverse relationship of neuroleptic dose with WAIS-R summary scores as well as with several subtests. Verbal memory was additionally related to medication level. Performance on the Trial-Making 'B' test was positively associated with neuroleptic dose, perhaps because the medication may have freed the subjects from competing internal stimuli thereby allowing them the attention to shift set between sequences.

Both subject's age and years of illness were associated with motor speed and verbal retrieval. However, subject's age was additionally related to constructional skills. Length of hospitalization was not correlated with any one specific cognitive domain. Rather, it was associated with attention, motor speed, and phonemic discrimination. The motor control variables (ERS & AIMS), included to measure the influence of neuroleptic induced motor dyscontrol on neuropsychological test performance, was predictably associated with several tasks involving motor functioning. However, they were also related to verbal retrieval and to pre-representational modes of thinking (Color/Form Preference Test - CDB).

Correlation of neuropsychological measures with MARS Factors

An analysis of neuropsychological variable correlates of individual MARS Factors revealed only one significant relationship. Specifically, emotional unrelatedness (MARS

Table 24

Significant Neuropsychological Test Correlates of Subject Characteristics

Subject Characteristics	r
Demographic Variables	
Age	
Stick Test	-.43*
Letter Cancellation (time to completion)	.66+
Visual Confrontation Naming	-.38*
Trail-Making 'A'	.54*
Education	
Full Scale IQ (WAIS-R)	.59***
Verbal IQ (WAIS-R)	.61***
Performance IQ (WAIS-R)	.47**
MQ (WMS)	.58***
Mental Control Subtest (WMS)	.65+
Memory for Passage (WMS)	.51**
Trail Making Test 'A'	-.62***
Trail Making Test 'B'	-.49**
Stroop Test	.46**
Raven's Progressive Matrice	.56**
Stick Test	.52**

continued

Table 24 (continued)

Significant Neuropsychological Test Correlates of Subject Characteristics

Subject Characteristics	r
Education (continued)	
Money Road Map	.76+
Benton Visual Rentention Test (#Errors)	-.40*
Letter Cancellation Test	-.55**
Buschke list-learning Test (Av. per Trial)	.69+
Buschke list-learning Test (Recognition)	.51**
Token Test	.51**
Benton Facial Recognition	.40*
Hooper Visual Organization Test	.49**
Historical Variables	
Age of Onset	
Full Scale IQ (WAIS-R)	.37*
Performance IQ (WAIS-R)	.54**
Years of Illness	
Trail Making 'A'	.54*
Letter Cancellation	.50**
Sentence Repetition	.41*

continued

Table 24 (continued)

Significant Neuropsychological Test Correlates of Subject Characteristics

Years of Illness (continued)	
Visual Confrontation Naming	-.47**
Treatment Variables	
Days of Hospitalization	
Purdue Pegboard (Right Hand)	-.42*
Wepman Auditory Discrimination Test	-.48**
Neuroleptic Dose	
Full Scale IQ (WAIS-R)	-.46**
Verbal IQ (WAIS-R)	-.43*
Performance IQ (WAIS-R)	-.46**
Trail-Making 'B'	.46**
Buschke list-learning Test (Av. per Trial)	-.39*
Buschke list-learning Test (Recognition)	-.42*
Visual Confrontation Naming	-.39*
ERS	
Purdue Pegboard (Left Hand)	-.47**
Letter Cancellation	.46**
AIMS	
Visual Confrontation Naming	-.39*

continued

Table 24 (continued)

Significant Neuropsychological Test Correlates of Subject Characteristics

Note.

*$p<.05$; **$p<.01$, ***$p<.001$; +$p<.001$

All values are PM coefficients, two-tailed (See appendix for individual neuropsychological test degrees of freedom).

Factor 1) and expressive immobility (MARS Factor 2) were both found to be inversely related to verbal fluency ($r = -.57$, $df = 28$, $p < .01$ and $r = -.41$, $df = 28$, $p < .05$ respectively). Inappropriateness of affect (MARS Factor 3) was not related to any of the neuropsychological variables. It should be noted that emotional unrelatedness and expressive immobility were both related to "core" negative symptoms (PANSS Factor 1) ($r = .75$, $df = 28$, $p < .0001$ and $r = .59$, $df = 28$, $p < .001$ respectively). This is interesting in light of a significantly poorer negative versus positive group performance on verbal fluency reported earlier in this chapter.

Cognitive Developmental Performance

Correlation of cognitive developmental tasks with PANSS scores and factors

It was hypothesized that cognitive development would vary as a function of the relative prevalence of positive and negative symptoms in such a way that the greater the negative scale score, the lower the scores on cognitive developmental tasks. A dimensional analysis revealed that neither PANSS Positive Scale nor PANSS Negative Scale summary scores were associated with performance on any of the cognitive developmental tasks. In addition, no significant relationships were found in correlations between the three PANSS factors derived from a Principal Components Analysis and cognitive developmental tasks. Finally, no significant relationships were found between any of the individual PANSS Positive or Negative Scale items and cognitive developmental task performance. Thus, the hypothesized relationship between negative scale scores and cognitive development was not confirmed.

Correlations of cognitive developmental measures with subject characteristics

Correlations of each of the cognitive developmental tasks to age, education, age of onset, years of illness, days of hospitalization, chlorpromazine equivalence, and motor sample characteristics (Extrapyramidel Rating Scale and the Abnormal Involuntary Movement Scale) are shown in Table 25.

It was hypothesized that the cognitive developmental performance of subjects would be positively related to age of onset and to educational attainment. This hypothesized relationship was not confirmed as neither age of onset nor educational attainment was significantly related to any of the cognitive developmental tasks. Despite this, a slowing of psychomotor rate was predictably associated with age, years of illness, and scores on the Extrapyramidal Rating Scale. The Extrapyramidal Rating Scale, one of the motor control scales, was also found to be negatively associated with a cognitive developmental task which examines pre-representational modes of thinking.

Correlation of Manifest Affect Rating Scale Factor Scores with cognitive developmental variables

The possible influence of affective impairment on performance during cognitive developmental evaluation was investigated with a correlational analysis. No significant relationships were found between MARS factors and cognitive

Table 25

Significant Subject Characteristic Variable Correlates of Cognitive Developmental Measures

Cognitive Dev. Variable	r
Color-Form Scale	
Extrapyramidal Rating Scale	-.38*
Representational Total	NS
Egocentricity of Thought	NS
PEDT Mental Age	NS
SOA Psychomotor Rate	
Age	-.40*
Years of Illness	-.44*
Extrapyramidal Rating Scale	-.56*

*$p < .05$, df = 28, two-tailed.

developmental tasks. However, a significant relationship was noted between inappropriateness of affect (MARS Factor 3) and psychomotor rate ($r = .42$, df = 27, $p < .05$).

Discussion

Summary of Findings

This research was conducted in order to address several hypotheses regarding positive and negative syndromes in schizophrenia. The examination of these hypotheses utilized both a dichotomous (positive group membership versus negative group membership) and dimensional (degree of positivity versus degree of negativity) approach. Specifically, it was hypothesized that (1) both positive and negative groups would appear to be cognitively impaired based on neuropsychological test performance; (2) both negative group membership as well as a relatively greater degree of negativity than positivity would be associated with more impairment on those neuropsychological tests which assess anterior dysfunction; (3) Both negative group membership and a relatively greater degree of negativity than positivity would be associated with lower scores on cognitive developmental tasks; (4) Both negative group membership as well as a greater degree of negativity than positivity would be associated with subject characteristics including an earlier age of onset, less education, greater duration of illness, longer hospitalization, and a greater degree of motor abnormalities; (5) General intellectual capacity (FSIQ) and cognitive developmental performance of the sample would be positively correlated to age of onset and educational attainment; and (6) Both positive and negative syndrome subjects would display a disturbance of affect with the negative group as well as a greater degree of negativity than positivity being associated with emotional unrelatedness and expressive immobility while the positive group and a greater degree of positivity than negativity being associated with inappropriateness of affect.

An analysis of individual PANSS symptoms and summary scores yielded evidence suggesting that positive and negative symptoms may be neither homogenous within their own sets nor definitive of dichotomous subtypes. Furthermore, evidence was obtained which suggests that they are not mutually exclusive and that differences between the groups of symptoms do in fact exist. Three factors were generated through a principal components analysis (PCA): a "core" positive symptom factor, a "core" negative symptom factor, and an excitable/cognitive factor. As expected, the positive and negative groups were significantly different on the first two factors with no significant difference being noted on the third factor. Thus, the excitable/cognitive factor represents overlap between the groups.

During dichotomous (group) analysis, no significant differences between groups were noted in their relationship to demographic, historical, or treatment related subject variables. However, dimensional (relative degree of positivity and negativity) analyses revealed that higher positive scores were related to an earlier age of onset. Also noted was a significant positive relationship between degree of negativity and neuroleptic dose.

An analysis of the association of PANSS Scale symptoms and summary scores as well as PANSS factors to subject variables revealed several interesting significant relationships which will be discussed in this chapter.

An examination of the relationship of the PANSS to the SAPS and the SANS revealed that the PANSS Positive Scale summary score was significantly related to the SAPS and the PANSS Negative Scale was significantly related to the SANS. The PANSS Composite Scale was additionally found to be related to the SAPS-SANS score with no significant cross-correlations being noted, thereby establishing the criterion validity of the PANSS.

An examination of neuropsychological performance did yield a group difference, that of a significantly better positive than negative group performance on verbal fluency, a test of anterior functioning. A dimensional analysis of individual PANSS symptoms and summary scores revealed that the hypothesized greater degree of anterior dysfunction amongst the negative group was partially supported to the extent that a greater number of negative versus positive symptoms and summary scores were associated with anterior dysfunction. In adduition, a "core" negative symptoms factor derived from a PCA was found to be inversely related to Full Scale and Verbal I.Q.'s as well as to verbal fluency. The "core" positive symptoms factor was inversely related to right-handed performance on the Purdue Pegboard and the excitable/cognitive factor was inversely related to verbal memory, constructional skills, and attention. An analysis of the influence of subject characteristics on neuropsychological performance revealed that verbal skills appeared to be positively related to educational level while overall intellectual capacity was positively related to both educational level and to age of onset. Neuroleptic dose was found to be inversely related to WAIS-R summary scores, verbal memory, and to performance on the Trail-Making 'B' Test. Both subjects' age and years of illness were inversely associated with motor speed and verbal retrieval. Scores on the motor control variables were predictably associated with a poorer performance on several tasks involving motor functioning. Other neuropsychological tests will be discussed.

An analysis of performance on cognitive developmental tasks failed to reveal any significant positive-negative group differences as hypothesized. In addition, no significant PANSS symptoms nor PANSS factor correlations were noted with performance on these same tasks. Next, cognitive developmental measures were unrelated to subject variables and to affective state. Finally, cognitive developmental performance was additionally found to be unrelated to age of onset and educational attainment as hypothesized.

Impaired affect has been considered to be an integral part of the schizophrenic syndrome and thus subjects were clinically evaluated on the MARS. The negative groups displayed a greater degree of emotional unrelatedness and expressive immobility while the positive group was found to display a greater degree of inappropriateness of affect. The relationship of the MARS to individual PANSS Scale symptoms and summary scores was also investigated and will be discussed.

The influence of affect on neuropsychological test performance was also analyzed. Both emotional unrelatedness (MARS Factor 1) and expressive immobility (MARS Factor 2) were both found to be inversely related to verbal fluency. It should be noted that these factors were also significantly related to the "core" negative symptoms factor of the PANSS.

Implications

The Positive/Negative Dichotomy

The basic distinction between positive and negative symptoms as proposed by Andreasen and Olsen (1982) was not supported by the results of this study. Specifically, correlations between positive and negative symptoms were not negative as would have been expected if these symptoms represented opposite ends of a continuum. In addition, the sets of symptoms did not, on the whole, relate to other subtyping measures in ways which were hypothesized. Specifically, none of the hypothesized relationships were found to be significant between positive and negative syndromes and demographic, historical, or treatment related subject characteristics

Relationship of PANSS to other subtyping measures

While the PANSS (Kay et al., 1987) is becoming increasingly popular as indicated by its translation into thirteen foreign languages and being chosen as the positive and negative symptom rating instrument for a diagnostic training videotape program underwritten by Janssen Pharmaceutical, Inc. (Janssen Pharmaceutical, Inc., 1989), the SANS (Andreasen, 1983) and the SAPS (Andreasen, 1984) remain the more frequently used positive and negative symptom rating scales. As previously discussed (see Chapter 2), the PANSS was chosen for the phenomenological assessments in this study because it addresses many of the limitations shared by other rating instruments presently available. However, given their current popularity, the SAPS and SANS were utilized on the present subject sample in order to provide a measure of criterion validity. The pattern of intercorrelations amongst PANSS Positive and Negative Scales with the SAPS and SANS indicates that the PANSS provides an excellent assessment of positive and negative symptoms while additionally providing a measure of general psychopathology and a relative degree of intrasubject positivity versus negativity.

Consistency of positive and negative symptoms

The pattern of intercorrelations amongst PANSS Positive and Negative Scale symptoms (Table 13) suggest that positive and negative syndromes were not homogeneous in the present sample. In fact, of forty-nine intercorrelations amongst scale symptoms, only two significant negative correlations were obtained. Predictably, scores on excitement (Positive Scale) and blunted affect (Negative Scale) and difficulty with abstract thinking (Negative Scale) were inversely related. In addition, while the PANSS Positive Scale summary score and the PANSS Negative Scale summary score were not found to be inversely related, their positive association was quite small ($r = .13$, $p > .10$), thus indicating that these two scales are tapping independent symptom dimensions in schizophrenia. Thus, the proposal that positive and negative phenomenological subtypes as put forth by Andreasen and Olsen (1982) was not supported by these results. Perhaps more to the point is the fact that, while PANSS Positive and Negative Scales are statistically independent, they are not mutually exclusive. Support for this proposition has come from a number of studies in which the majority of schizophrenic subjects have been classified as demonstrating both positive and negative symptoms ("mixed type") rather than as falling exclusively into positive or negative categories (Andreasen & Olsen, 1982; Kay &

Opler, 1987a; Lindenmayer et al., 1984; Opler et al., 1984). Plausible explanations of the "mixed type" phenomenon can be found in the literature. For instance, Andreasen (1985) has proposed the following explanations as to why some schizophrenics do not fall neatly into either the positive or negative phenomenological categories: (1) the "mixed" patient may actually be enroute from an original positive state to a negative state; (2) imbalances of multiple neurochemical systems may lead to a "mixed symptom" picture; and (3) "mixed" patients may suffer from multiple involvement of different cerebral regions which, depending on the specific foci affected, may result in a mix of both positive and negative symptoms.

Relationship of subject characteristic variables to phenomenology

When subjects were dichotomously classified into either positive or negative groups and compared on subject characteristics, no significant relationships were apparent. This lack of significant differences on group membership may be attributable to two factors. First, it may be due, at least in part, to the fact that state psychiatric patients tend to have somewhat homogeneous backgrounds. As an example, a significant number tend to come from lower socioeconomic backgrounds. Such a background might be expected to influence several of the subject characteristics. As an example, age of onset could be influenced by a family who was committed to deal with a family member's "eccentric" behavior for as long as possible before seeking out psychiatric treatment for him. This issue may be addressed by including subjects from various socioeconomic levels in future studies. The second and more likely explanation, however, is that none of the subjects in this study were either exclusively positive nor negative. Rather, varying degrees of both positive and negative symptoms were noted in all of the subjects. It might then be the case that several significant subject characteristic differences might become apparent during a dimensional analysis. This turned out to be the case with degree of positivity versus negativity being related to two subject characteristics. Specifically, age of onset was inversely associated with conceptual disorganization, hallucinatory behavior, and suspiciousness (PANSS Positive Scale symptoms) and with stereotyped thinking (PANSS Negative Scale symptom). Given that conceptual disorganization and stereotyped thinking were related ($r = .72$, $p < .001$) and reflect two of the three PANSS items related to cognitive functioning, one might interpret this inverse relationship with age of onset as reflecting incomplete cognitive development. However, this interpretation is difficult to support given that there were no significant relationships between any of the cognitive developmental tasks and age of onset. Despite this, the finding that both conceptual disorganization and stereotyped thinking were significantly associated with performance on the Wisconsin Card Sorting Test, suggests that these symptoms may represent incomplete prefrontal development and that either the cognitive developmental tasks or the sample size used in this study were not sensitive enough to uncover what may be subtle signs of incomplete cognitive development.

In addition to the individual symptoms, the PANSS Positive Scale summary score was associated with an earlier age of onset and the PANSS Negative Scale summary score was associated with a higher neuroleptic dose. While this relationship of positivity to age of onset is contrary to that found in many studies, it is possible that the age of onset was simply more obvious and memorable in that group because of productive symptoms. That is, perhaps those subjects with a predominance of negative symptoms were simply "maintained" at home until they became unmanageable whereas the hallucinations and delusions of the more positive subjects brought them to clinical attention at an earlier age. The fact that degree of negativity was directly related to neuroleptic dose may reflect the possiblility that the negative syndrome is, at least in part, neuroleptic exacerbated. It could, of course, also be attributable to negative syndrome patients being more neuroleptic resistant, thereby leading to trials on higher doses.

Neuropsychological Performance

While within the borderline range, the overall intellectual capacity of the present sample was within the range typical of schizophrenic populations (Payne, 1973) and consistent with that found in other studies of this population (Bilder, 1985; Kay, 1979). In addition, this sample also demonstrated a significantly greater Verbal than Performance IQ ($t = 4.55$, $df = 28$, $p = .0001$, two tailed). This finding is also consistent wih other findings which show that schizophrenics are characterized by a greater verbal than performance IQ (Kay, 1979; Payne, 1973). It is possible that two factors may account for this finding. First, a majority of tests comprising the performance subtests of the WAIS-R are timed and therefore scores on these tests are influenced by the slowing effect of neuroleptic medication. Secondly, the verbal scale subtests include a greater number of items which are dependent on "old learning" and, therefore, may be resistant to cognitive disruption later on.

Several of the tests included within the neuropsychological battery are widely used as "screening" instruments for the identification of brain damage. When performance on these tests was analyzed, from 22-85% of the sample received scores low enough to warrant a classification of brain-damaged. Two of these screening instruments were also utilized in a previous study of positive and negative symptoms in a similar population of schizophrenics (Bilder, 1985). In that study, 70% of the subjects were classified as being brain-damaged on the basis of their performance on the Trail-Making Test, Part 'A' while 78% of the subjects failed to meet cutoff score requirements for Part 'B' of the same task. These scores are consistent with those of the subjects in the present study, where 76% and 85% failed to reach cutoff criteria for Parts 'A' and 'B' respectively. When the performance of subjects classified as either positive or negative on this test was compared, no significant differences were apparent. Thus, while the present sample as a whole did poorly on both parts of the Trail-Making Test, a task known to be sensitive to anterior dysfunction, neither positive nor negative group performed significantly poorer than the other. This raises the suspicion that both positive and negative schizophenic patients may display some degree of anterior dysfunction indicating that, contrary to Crow's (1980) original model, the positive syndrome may also have a neurological underpinning. Despite this, when group differences were examined across all neuropsychological variables, only verbal fluency, a task known to be sensitive to left anterior dysfunction (Milner, 1967a; Miceli et al., 1981; Perret, 1974), yielded a significant difference in performance by positive and negative groups. Specifically, the negative group did not perform as well as the positive group on this tasks ($t = 2.12$, $df = 26$, $p < .05$). It would seem then that while there is some evidence supportive of anterior dysfunction in both positive and negative groups, the negative group appears to display a greater disruption of left anterior functioning.

It should be noted that lack of group differences across a majority of neuropsychological tasks is most probably attributable to the fact that the present sample was representative of an impaired group as a whole. Thus, any significant subtype differences might require a much larger sample size.

Relationship of PANSS items to neuropsychological variables

An analysis of the significant neuropsychological test correlates of individual PANSS scale items was more revealing than positive and negative group comparisons. Conceptual disorganization, the one cognitive symptom of the

PANSS Positive Scale, was inversely related to both general indices of cognitive integrity as well as to prefrontal impairment as assessed with the Wisconsin Card Sorting Test (WCST). It was also found to be inversely related to verbal memory. Another Positive Scale symptom, hallucinatory behavior, was inversely associated with bilateral motor functioning. Thus, two of the seven PANSS Positive Scale symptoms were significantly related to impaired anterior functioning. In addition, the overall PANSS Positive Scale summary score was also significantly associated with anterior dysfunction. Specifically, it was associated with a decrement of right-handed motor functioning. Evidence was therefore obtained which suggests that anterior and left hemisphere dysfunction is associated with degree of positivity. Despite this, other individual positive symptoms were found to be related to visual-spatial impairment, thus implicating right hemisphere functioning as well.

As was the case with the PANSS Positive Scale, the one cognitive symptom of the PANSS Negative Scale, stereotyped thinking, was also inversely related to general indices of cognitive integrity, to prefrontal impairment as assessed by the WCST, and to verbal memory. While it is tempting to ascribe poor performance on tasks which tend to assess anterior dysfunction in this sample to an overall impairment of cognitive functioning and to ignore phenomenological correlates, it should be noted that six out of seven PANSS Negative Scale symptoms were significantly related to a decrement of anterior functioning. The overall PANSS Negative Scale summary score was additionally related to a decrement of anterior dysfunction as well as to an impairment of overall intellectual integrity.

A greater degree of PANSS Negative versus Positive Scale impairment on tests known to be sensitive to Left Hemisphere impairment was also found during the analysis of individual PANSS items. Specifically, thirteen of sixteen (81%) significant neuropsychological variable correlates of PANSS Negative Scale items were consistent with left hemisphere compromise as opposed to four of nine (44%) neuropsychological variable correlates of PANSS Positive Scale symptoms. While not directly related to positive and negative symptoms per se in the literature, this finding is consistent with a number of studies which have found evidence of left hemisphere dysfunction in schizophrenia (Abrams et al., 1981; Flor-Henry, 1976; Flor-Henry et al., 1983; Gruzelier & Hammond, 1976; Newlin et al., 1981). In a review of studies examining laterality and hemispheric dysfunction in schizophrenia, Nasrallah (1982) found considerable evidence of lateralized left hemisphere dysfunction in schizophrenia. What is more pertinent to the present study is the fact that Nasrallah's review led him to conclude that the temporal-frontal region was one of the left hemisphere areas most likely to be involved in this dysfunction. This is certainly consistent with the presence of left hemisphere and frontal dysfunction in the present sample.

Relationship of subject characteristics and affect to neuropsychological variables

An analysis of significant subject variable correlates of neuropsychological test performance revealed that age of onset was positivity related to Full Scale and Performance IQ's. This may indicate that, while positive and negative groups did not significantly differ on education, perhaps an earlier age of onset was related to incomplete cognitive development, at least in some schizophrenics, as has been proposed in the literature (Opler et al., 1984), thereby leading to a lowering of IQ. Contrary to this, no significant relationships were noted between cognitive developmental tasks and age of onset. However, once again, it is possible that an earlier age of onset of the schizophrenic illness may have affected cognitive maturity in subtle ways that were beyond either the sensitivity of the cognitive developmental tasks employed in this study or were subtle enough not to be detected because of the sample size.

Predictably, education was related to performance on neuropsychological tests tapping a variety of cognitive functions. It was however, also related to Full Scale, Verbal, and Performance IQ's. Thus, while verbal skills seem related to educational level, overall intellectual capacity seems related to both education as well as to age of onset.

While performance on an alternating sequencing task, Trail-Making 'B,' was predictably slowed by increasing neuroleptic dose, performance on Trail-Making 'A,' a simple sequencing task, was not. In fact, neuroleptic dose was unrelated to any of the simple sequencing tasks in the neuropsychological battery. This is interesting in light of the possible role of neuroleptics in correcting sequencing deficits which may be part of the schizophrenic disorder. Specifically, borrowing from the work of Nauta, Eliot Gardner (1987) has speculated that nigrostriatal hyperdopminergia leads to sequencing problems which neuroleptics can correct. The reason that performance on Trail-Making 'B' was not enchanced in relationship to neuroleptic dose may be that it does not represent a simple sequencing task. Rather, it is more complex in the sense that it additionally requires the maintenance and alternation between two different sequences. Thus, Gardner's proposition may have relevance here. Neuroleptics, therefore, may help enhance the performance of specific cognitive tasks as previously proposed in the literature (Baker, 1968; Small et al., 1972). Despite this, they may also hinder performance on other cognitive tasks (for a review, see Medalia et al., 1988). As an example, larger neuroleptic dose was related to a lower overall intellectual capacity as measured with the WAIS-R as well as with a poorer performance on a selective reminding verbal memory task. This is somewhat contrary to findings in the literature of neuroleptic related improvement in IQ scores (Depue et al., 1975; Kovitz et al., 1955). However, these differences may be attributed to medication and sample differences. As an example, half of the Kovitz et al. (1955) sample were receiving maintenance ECT treatment during the study. It should also be noted that none of these studies controlled for practice effects.

The inverse relationship of neuroleptic dose and verbal list-learning and recognition is consistent with findings of Medalia et al. (1988) who, in a review of the literature, found that the weight of recent evidence supports a negative drug effect on recall and may impair verbal recognition as well.

The finding of an inverse association between left-handed fine motor speed (Purdue Pegboard) and extrapyramidal signs is consistent with the result of two studies in which a significant relationship was found between a decrement in Purdue Pegboard performance and EPS (Pear, 1962; Rosofsky et al., 1982). It should be noted, however, that impaired performance on the Purdue Pegboard in the present sample was limited to left-handed performance. While it is difficult to explain why right-handed performance on the Purdue Pegboard was not affected by extrapyramidal signs, perhaps the dominant hand (the present sample was right dominant) is less affected by a mild degree of EPS than the nondominant hand, at least on this task. An alternative explanation, though speculative, is that poorer left-handed performance on the Purdue Pegboard might be attributable to subtle parkinsonian side effects of medication. Such side effects may have been too subtle to be apparent during evaluation with the ERS and AIMS. If one accepts this proposition, the explanation becomes rather evident. Specifically, it is known that parkinsonian inertia becomes less problematic with use. Since this exclusively right-handed sample would have used their right hand to complete several of the neuropsychological tests prior to taking the Purdue Pegboard test, the subtle parkinsonian side effect of initial inertia may have had a greater impact on left-handed performance. Scores on the ERS were also found to be predictably related to poorer performances on speeded motor tasks. However, it is unclear as to why the motor control scales were additionally related to verbal retrieval and to pre-representational modes of thinking.

Age at the time of neuropsychological assessment was positively associated with a slower performance on timed motor tasks, as might be expected.

As reported in the previous chapter, the relationship of affect to neuropsychological variables was such that emotional unrelatedness (MARS Factor 1) and expressive immobility (MARS Factor 2) were inversely related to verbal fluency. Both of these factors were also related to the PCA derived "Core" Negative Symptoms Factor. This is consistent with the poorer negative versus positive group performance which was found during an examination of verbal fluency. It may well be that the emotional unrelatedness and expressive immobility of the negative syndrome would inhibit verbal productivity.

Cognitive Developmental Performance

Both dichotomous and dimensional analyses of the relationship of positive and negative symptoms to performance on cognitive developmental tasks failed to reveal any significant relationships. This was also found to be the case when reviewing the association of PCA derived PANSS Factors to cognitive developmental task performance.

Given rather consistent findings of cognitive developmental impairment amongst schizophrenic patients (Kay et al., 1975a,b), it is unclear as to why such deficits were not apparent in the present sample. While it is tempting to hypothesize that this was the result of poor intellectual functioning in this group, the sample as a whole obtained WAIS-R IQ scores which were similiar to that found in the general schizophrenic population. However, when one examines those studies which have found evidence consistent with cognitive developmental impairment in schizophrenia, certain differences between those studies and the present one may serve to explain the lack of such findings in this study. Specifically, studies in which significant correlations were found between cognitive developmental impairment and a diagnosis of schizophenia have employed larger samples of patients than was the case in the present study. For example, Kay's work has included samples of 59 (Kay & Singh, 1975a) and 63 patients (Kay, 1982). More recent studies have found significant differences between positive and negative subjects, as determined by the PANSS, on certain components of the Cognitive Diagnostic Battery (CDB). In a 1986 study of 101 schizophrenic patients, Kay and his colleagues found significant inverse relationships between scores on the PANSS Negative Scale and performances on the Colour-Form Preference (CFP) and Egocentricity of Thought (EOT) subtests of the CDB. The CFP examines pre-representational modes of thinking while the EOT consists of hierarchically arranged subtests which assess the maturity of right-left positional concepts (Kay & Singh, 1975b). This same inverse relationship was also noted on the Span of Attention (SOA) subtest of the CDB (psychomotor rate). Two studies reported by Opler et al. (1987) review, amongst other findings, the results of typological versus dimensional assessment of the relationship of positive and negative symptoms to cognitive developmental performance on the CDB. The first was a study of 47 schizophrenic patients typologically classifed as positive or negative in which the majority of negative patients utilized a more primitive conceptual style that the positive patients in completing the CFP subtest of the CDB (Opler et al., 1984). The negative patients were additionally found to be significantly slower than the positive patients on a measure of psychomotor rate. Another study reported on by Opler et al. (1987) was conducted on a sample of 101 schizophrenic subjects who were classified dimensionally according to degree of positivity and negativity on the PANSS. As was the case in the Opler et al. (1984) study, degree of negativity was significantly related to impaired performances on both the CFR and EOT subjtests of the CDB (Kay, et al., 1986). Thus, the lack of significant cognitive developmental findings in the present study may be related to the small sample size relative to the studies cited above. This may have caused a lack of sufficient variation in CDB scores to yield significant cognitive developmental differences between positive and negative groups.

Implications of developmental theory

The search for an etiological explanation for the occurrence of positive and negative symptoms has led to an increased interest in possible neurodevelopmental factors which may be related to the development of these symptoms. Weinberger (1986, 1987) has, in fact, proposed a neurodevelopmental theory of schizophrenia. He has proposed that early developmental pathology, particularly affecting the dorsolateral prefrontal cortex (DLPFC), eventually leads to schizophrenic symptoms when affected neural systems reach maturity in early adulthood. He cites neuropathological evidence in support of early pathological events leading several investigators to suspect a congenital lesion in the schizophrenic disorder (Benes et al., 1986; Bogerts, et al., 1985; Jakob & Beckman, 1986; Kovelman & Scheibel, 1984). Since the manifestation of an early "lesion" is dependent on the state of cerebral maturation (Adams & Lyons, 1982) and the DLPFC is the most ontogenetically recent cerebral structure to begin myelination (Yakovles & LeCours, 1964), it is possible that very early cerebral compromise affecting this region would not lead to overt behavioral manifestations until early adulthood. This, of course, coincides with the usually reported schizophrenic age of onset and would be consistent with a "critical period of vulnerability for the expression of psychotic behavior" (Weinberger, 1987, p. 662). The existence of critical periods for the developmental of certain functions, such as certain aspects of vision (Hubel & Weisel, 1965) and language (Lenneberg, 1967), are well known and so the possibility of a "maturational window" for the development of adult onset schizophrenia is certainly plausible, although such a hypothesis may need to propose different neurodevelopmental processes to explain the early onset of childhood schizophrenia.

Weinberger's proposition of a neurodevelopmental compromise of the DLPFC could account for what are considered negative or defect symptoms: affective flattening, social withdrawal, apathy, difficulty learning from past experience. However, DLPFC compromise would not account for positive or productive symptoms, as these are more likely to be associated with limbic and diencephalic overactivity (Davison, 1983; Davison & Bagley, 1969). Weinberger views positive symptoms as resulting from mesolimbic dopaminergic hyperactivity, which is a secondary result of the neurodevelopmental pathological process he ascribes to the negative syndrome. As evidence in support of this view, Weinberger cites postmortem studies which have found increased numbers of limbic postsynaptic D_2 dopamine receptors (Crow, 1980; Seeman, 1984; Weinberger & Kleinman, 1986). This finding may not simply reflect an epiphenomenon associated with a history of having received neuroleptic treatment as indicated by the finding of increased striatal dopamine receptor activity in medication-naive patients (Wong et al., 1986). Thus, Weinberger's neurodevelopmental theory proposes that negative or defect symptoms reflect the neurodevelopmental manifestation of an early developmental cerebral insult resulting in mesocortical dopaminergic hypoactivity. Positive symptoms, on the other hand, are attributable to mesolimbic dopaminergic hyperactivity which may be the result of prefrontal dopaminergic deafferentation with subsequent disinhibition of subcortical dopamine tracts.

Evidence in support of this proposition comes from a study of rats in which prefrontal dopamine afferents were selectively destroyed leading to chronic subcortical dopamine hyeractivity (Pycock et al., 1980). An obvious difficulty with using these results to support this contention is that evidence does not yet exist which indicates that human and rat brains are neurally "wired" in an analogous fashion as regards prefrontal-subcortical interrelationships. Another problem with Weinberger's proposed neurodevelopmental theory is that it presupposes a single etiolgic source, the DLPFC "lesion," to account for both negative and positive symptoms. One would then expect a significant direct relationship between positive and negative symptoms. The relationship between positive and negative symptoms in the present sample was found to be quite weak and nonsignificant (r = .13), thus unsupportive of Weinberger's theory. Of course, it is quite possible that there is some merit to Weinberger's proposal and that there are, in actuality, two, as of yet undetermined, "lesions" of neurodevelopmental origin, one of which predominantly affects the DLPFC while the other leads to mesolimbic dopaminergic hyperactivity. A speculative example would be that neuroleptic nonresponders do indeed suffer from dopaminergic dysfunction, however such dysfunction may be compounded by anterior structural compromise. Goldberg (1985) has pointed out that not all negative schizophrenics are neuroleptic nonresponders. Rather, it is those negative syndrome patients who present with ventricular dilation who tend to be nonresponders. Thus, a multifactorial etiologic view of schizophrenia may be a more fruitful approach to understanding the roots of this disorder.

Alternatively, one should not neglect the importance of individual differences in any etiologic theory of positive and negative symptoms. Perhaps a single "lesion" as proposed by Weinberger could, in fact, account for the appearance of positive and negative symptoms. Should that be the case, such a developmental lesion would be then expected to interact with environmental stressors, which are thought to affect neuronal structure (Haracz, 1985; Kandel, 1983). Therefore, while quite speculative, even starting from a single DLPFC "lesion" as in Weinberger's model, various environmental influences might cause differences in cortical development in such a way as to lead to a relative preponderance of positive or negative symptoms or even to a "mixed" phenomenological presentation. The poorer premorbid history which seems typical of the negative subtype schizophrenic may, in fact, be a by-product of environment stressors which, in the short run, lead to maladaptive psychosocial responses but in the long run, depending on the age in which such stressors are experienced, lead to developmental impairment of neurophysiological mechanisms which would take longer to manifest itself. Should this be the case, programs of cognitive and psychosocial skills training with high-risk children may lead to the alleviation of or even prevent the full development of schizophrenic symptoms, perhaps to the point where individuals who would normally fall into the poor prognosis category would actually become good outcome schizophrenics during adulthood or might not develop the full-blown schizophrenic syndrome at all. The positive effects of social skills training and occupational therapy in lessening recidivism rates among schizophrenics is becoming well known (Liberman et al., 1986; Linn et al., 1979). Cognitive retraining of such individuals has also been proposed (Yozawitz, 1986). Unfortunately, such intervention strategies are utilized after the development of the schizophrenic illness. It would be most interesting if such training could mediate the environmental demands or at least the individual's capacity to deal with such demands and, therefore, the stress side of the diathesis-stress equation on an already developmentally compromised organism prior to the onset of schizophrenia.

Generalizability of Findings

Sampling considerations

In comparing the results of the present study to that of previous investigations, similarities of the samples utilized must be considered. The subject population used in the present study was similar in several basic respects to that employed in a number of prior studies. Specifically, the mean scores and age distribution corresponded to that of most other samples which have been studied with similar methods (e.g., Andreasen & Olsen, 1982; Bilder, 1984; Dewan et al., 1983; Donnelly et al., 1980; Jeste et al., 1982; Nasrallah et al., 1982). As is true in any sample of schizophrenics, age of onset tends to be relatively consistent, and the age of onset found in the present sample (mean = 20.8 years) is fairly representative. There are, of course, studies where the sample consists predominantly of subjects with an earlier onset. As an example, 65% of the patient sample in the Cannon-Spoor et al. (1982) study had an age of onset younger than 18 years. On the other hand, there are studies where the mean age of onset is somewhat older than in the present study (e.g., Andreasen et al., 1982; Nasrallah et al., 1983). As is true of age of onset, the range of education does not tend to differ significantly from sample to sample with the majority of schizophrenic patients having gotten as far as the 10th grade. Of course, a number complete their high school education with a few going on to college. The sample employed in this study is representative in these respects. In contrast, the duration of illness in the present smple (mean = 9.8 years) is somewhat less than that found in the Bilder (1984), Jeste et al. (1982), or Weinberger et al. (1979) studies. It is, however, somewhat more than that of most other studies where subjects have been ill for only four to seven years. Those studies where the duration of illness has been much longer have tended to include much older patients in their subject pool. While the overall level of psychopathology in the present sample was at the 50th percentile (General Psychopathology Rating Scale mean score = 40.13) when compared to a population of 240 medicated schizophrenic inpatients (Kay et al., in press), it is quite difficult to compare absolute levels of psychopathology across different samples. The major reasons for this are that few studies report on the absolute level of their subject's illness, while those that do tend to employ different rating instruments. Until more uniformity is achieved in the rating of overall psychopathology across samples, such ratings will continue to be most useful in comparing subgroups within a sample as was the case in the present study.

Comparability of experimental measures

The overall level of intellectual functioning in the present sample was low. In several published reports which specify IQ (e.g., Donnelly et al., 1980; Rieder et al., 1979), Full Scale IQ's have tended to be within the average range. As previously discussed, Full Scale IQ's were largely within the upper borderline range in the present sample. Performance IQ's were additionally within the borderline range with Verbal IQ's falling within the low average range. Despite this, other studies (e.g., Bilder, 1985) have used samples with Full Scale IQ's which were in the borderline range. Furthermore, when performance on tasks used for the identification of "organicity" was examined, a majority of subjects in the present sample were in the "brain damaged" range, as has been the case in several other studies (Bilder, 1984; Donnelly et al., 1980).

Conclusion

Many of the results presented here would not have been obtained if data had been analyzed exclusively within the framework of the hypothesized dichotomy between positive and negative syndromes as distinct schizophrenic syndromes. Rather, the majority of significant findings became apparent only after analyzing the influence of positive and negative symptoms on performance from a dimensional perspective across the entire sample.

It is noteworthy, however, that truncated sampling may have limited the number of significant findings in this study. As an example, all patients had a relatively poor prognosis according to standard clinical indications. Specifically, they were all somewhat refractory to neuroleptic treatment or they would not have had extensive psychiatric histories, including past psychiatric hospitalizations for extended periods. In fact, this seems to have held true for both positive and negative syndrome patients in this study, as significant differences were not noted between the two groups on days hospitalized. This was the case whether subject characteristic data were analyzed dichotomously or dimensionally. Futhermore, almost all subjects, both positive and negative, exhibited moderate-to-severe neuropsychological compromise.

If the nature of this sample is taken into account, then some of the present findings are, in fact, consistent with hypothesized relationships between positivity/negativity and neuropsychological functioning. Specifically dichotomous analyses revealed that negative group membership was associated with poor verbal fluency, a task related to left anterior functioning, whereas positive group membership was not. During dimensional analysis, the PANSS Negative Scale summary score as well as six of seven PANSS Negative Scale symptoms were significantly related to a decrement of anterior functioning. Despite this, there was also some evidence of a direct relationship between anterior dysfunction and positive symptoms. However, only two of seven PANSS positive symptoms were related to such dysfunction. Thus, while both syndromes are to some degree associated with anterior dysfunction, the negative syndrome is more consistently so. In fact, if one were to disregard performance on both the Purdue Pegboard because of the slowing effects of neuroleptic medication as well as WAIS-R summary scores due to the difficulty inherent in neatly attributing all verbal and performance subtests to either left or right hemisphere functioning, negativity becomes directly related to a predominance of left hemisphere and frontal dysfunction. Degree of positivity, on the other hand, was found to be related to frontal and bilateral dysfunction. Despite this, there were several tests of anterior function which failed to yield a significant differential performance between positive and negative groups during both dichotomous and dimensional analyses. Perhaps this is related to subtle differences which, because of sample size, did not become apparent.

In attempting to answer questions regarding the nature of positive and negative syndromes, several directions for future research have become apparent. The role of neuroleptics in neuropsychological performance needs to be addressed. While some have attempted to describe the influence of neuroleptics on specific cognitive skills (for a review, see Medalia et al., 1988), they have usually controlled for such influence by including drug withdrawn patients. Unfortunately, drug withdrawal is usually for only two or three weeks before testing. This may not be an adequate withdrawal period, as cogent arguments have been made in the literature regarding the possibility of residual drug effects well beyond a two to three week washout period (Cohen et al., 1988; Hubbard et al., 1987). In order to adequately address this issue, future studies should include first break schizophrenics who have never received neuroleptic treatment. Given that such patients are indeed difficult to find, patients who have been neuroleptic free for a minimum of six months (e.g., noncompliers) could provide a viable alternative.

Biological and electrophysiological measures should also be employed in future studies as their relevance to schizophrenia has been implicated (McCarley et al., 1989; Meltzer, 1987). As an example, McCarley and colleagues (1989) have been successful in establishing a direct relationship between the P200 auditory evoked potential, frontal CT abnormalities, and negative symptoms. Given the number of positive findings in studies which have utilized neuroimaging, electrophysiological, neuropsychological, and phenomenological techniques in elucidating differences related to positive and negative symptoms, it may well be that the most fruitful approach to studying the nature of positive and negative symptoms in schizophrenia will be one which employs multidisciplinary techniques on the same subjects.

The question as to whether poor neuropsychological performance is related to incomplete cognitive development or impairment of previously intact cognitive processes remains to be answered. Longitudinal assessments in high-risk samples and more through retrospective studies of developmental social and academic history are required to address this issue. An understanding of premorbid intellectual abilities might prove to be an indispensable advantage in interpreting current neuropsychological functioning.

As stated previously, most schizophrenic individuals can be expected to present with both positive and negative symptoms although a predominance of positive or negative symptoms can usually be established. Thus, future studies should concentrate on relationships involving the relative prevalence of positive and negative symptoms rather than viewing these syndromes as purely dichotomous in nature. The utilization of this approach to data analysis proved quite useful in arriving at the significant findings reported herein.

Finally, it is quite plausible that neuropsychological differences between positive and negative syndrome schizophrenics exist which are subtle. Therefore, samples displaying greater variability should be considered. Future studies should also employ larger numbers of subjects in order that such subtle differences might become more apparent. Larger numbers would also allow for more effective use of factor analytic techniques.

Appendix 1

Sample Characteristics on Subject Variables

Subject Variable	Mean	SD	Range Minimum	Range Maximum
Demographic Variables				
Age	30.17	7.74	20	56
Years of Education	10.30	2.68	5	16
Historical Variables				
Age of Onset	21.30	5.18	11	34
Years of Illness	9.80	7.40	1	38
Treatment Variables				
Days Hospitalized+	397.07	244.81	61	730
Neuroleptic Dose (mg.)++	968.00	597.64	0	2400
Motor Control Scales:				
ERS	11.90	10.99	0	32
AIMS	3.17	5.00	0	20

N = 30

+Within past 18 months

++CPZ Equivalence

Appendix 2

Individual Neuropsychological Test Degrees of Freedom

Neuropsychological Test	Degrees of Freedom
WAIS-R	28
Mental Control (WMS)	28
Memory for Passages (WMS)	28
Paired Associate Learning (WMS)	28
Total Raw Score (WMS)	28
Wisconsin Card Sorting Test	23
Verbal Fluency	26
Trail Making Test (A) Time	27
Trail Making Test (B) Time	27
Stroop Test	27
Raven's Progressive Matrices (A-C)	26
Purdue Pegboard (Left hand)	25
Purdue Pegboard (Right hand)	26
Purdue Pegboard (Bimanual)	25
Stick Test (Memory)	20
Money Road Map	25
Benton Visual Retention Test (BVRT)	27
Letter Cancellation Test	24
BVRT Recognition	23
Buschke (Av. Per Trial)	28
Buschke Recognition	25
Wepman Auditory Discrimination	27
Token Test	24

continued

Appendix 2 (continued)

Individual Neuropsychological Test Degrees of Freedom

Neuropsychological Test	Degrees of Freedom
Sentence Repetition Test	26
Visual Confrontation (BDAE)	26
Benton Facial Recognition	27
Hooper Visual Organization Test	27
CDB Color/Form Scale	27
CDB Representational Total	28
CDB Egocentricity Of Thought Test	28
CDB PFDT Mental Age	26
CDB Span of Attention (SOA)	27
CDB SOA Psychomotor Rate	27
Boston Apraxia	28

Appendix 3

Means and Standard Deviations of Neuropsychological Test Variables

	Sample		Positive		Negative	
Neuropsych. variable	Mean	SD	Mean	SD.	Mean	SD
FSIQ	77.6	10.9	79.2	10.0	75.6	10.4
VIQ	82.1	11.2	84.3	12.3	79.2	9.9
PIQ	74.9	10.7	75.5	10.1	79.0	11.9
Mental Control	5.2	2.4	4.9	2.8	5.2	1.7
Memory for Passages	6.2	3.6	6.4	3.3	6.1	4.1
Paired Associate Lrn.	9.7	4.6	9.8	4.6	10.1	5.0
Total Raw Score	49.7	13.6	47.3	14.3	52.5	13.3
WCST Persv. Errors	26.4	20.7	26.5	16.4	26.6	26.4
WCST Cat. Achieved	2.6	2.3	2.5	2.2	2.5	2.4
FAS	34.3	12.6	37.5	10.7	29.4	11.8
Trail A Time	66.2	36.8	75.3	45.0	57.7	23.8
Trail B Time	166.2	27.0	166.1	67.1	166.8	93.1
Stroop Total Score	24.5	6.3	25.4	5.7	23.4	7.1
Sum Raven's A-C	20.8	7.0	21.2	6.8	20.3	7.8
Purdue Left	12.7	2.4	12.8	2.0	12.6	2.9
Purdue Right	13.6	2.1	13.6	2.0	13.8	2.3
Purdue Both	10.4	2.0	10.4	2.0	10.6	2.2
Stick Test Memory	8.7	3.7	7.9	4.2	9.9	2.9
Money Road Map	23.2	6.5	23.5	6.4	23.0	7.0
BVRT # Correct	3.2	2.1	2.9	2.1	3.2	2.1
BVRT # Errors	11.8	5.9	12.1	6.4	12.1	5.2
Letter Cancellation	125.4	54.2	134.4	70.2	115.0	26.4
BVRT Recognition	6.1	2.2	6.2	2.1	5.9	2.3
Buschke Av. Per Trial	6.7	1.7	6.5	1.5	6.7	1.8

Appendix 3 (continued)

Means and Standard Deviations of Neuropsychological Test Variables

	Sample		Positive		Negative	
Neuropsych. variable	Mean	SD	Mean	SD	Mean	SD
Buschke Recognition	8.6	1.7	19.0	1.5	19.0	1.5
Wepman Total Correct	37.8	5.0	38.6	4.1	36.9	6.0
Token Test	33.3	8.2	32.4	5.2	34.3	10.9
Sentence Repetition	14.1	2.1	14.1	2.4	14.0	1.7
Visual Confrontation	100.3	9.2	100.1	10.6	100.0	7.8
Facial Recognition	42.0	7.8	42.7	7.1	40.9	9.0
Hooper	20.7	5.5	21.5	6.2	19.5	4.8
CDB Color/Form Scale	21.3	3.7	21.6	3.3	20.5	4.3
CDB Rep. Total	15.9	3.1	15.1	3.8	16.6	2.0
EOT	2.1	0.8	2.3	0.8	1.9	0.9
PFDT Mental Age	5.6	0.9	5.7	0.9	5.6	0.9
Span of Attention	204.0	135.5	192.4	143.1	187.4	119.5
SOA Psychomotor Rate	1.0	0.2	1.0	0.2	1.0	0.2
Boston Apraxia	12.4	2.0	12.1	2.6	12.6	1.4

Appendix 4

Consent Form

A copy of the actual consent form used in this study is shown on the following page. Please note that this consent form covers five procedures encompassing three studies, one of which was the study reported in this manuscript. The protocol procedures and consent form were approved by the Institutional Review Boards of Bronx Psychiatric Center and the New York State Office of Mental Health.

Appendix 4

Rev. 1-23-83

Bronx Psychiatric Center-Form For Informed Consent

Name of Researcher: Lewis A. Opler, M.D., Ph.D.
Title of Project: Syndromes in Psychiatric Inpatients
The purpose of the research is: To better understand and identify those syndromes which collectively comprise "nervous breakdowns" leading to hospitalization, but which may represent different underlying conditions.

Drugs and/or procedures involved: You will be asked to accept transfer to the Psychopharmacology Research Ward for a period of two to three months, where a series of evaluations will be undertaken, specifically: (1) interviews; (2) paper-and-pencil tests; (3) neurological evaluations, including getting a CAT scan (a painless and safe brain X-ray); (4) studies of eye movements, involving following a swinging pendulum, opening and closing your eyes, and looking at some dots. At one point during the evaluations, your medication will be slowly decreased, and, if possible, stopped.

Benefits expected: These evaluations are not treatments, so that you are unlikely to receive immediate benefit. However, the completenes of the evaluation may shed light on the nature of your condition which could help in planning your future treatment. Your participation will help increase knowledge regarding the different syndromes that collectively comprise major psychiatric disorders.

Possible risks involved: All of the evaluations involve safe procedures. During the period when your medication is being decresed and eventually stopped, you may experience some increase in the intensity of the symptoms which brought you into the hospital. Should this happen, necessary medication will be restarted.

I, ____________________, agree to participate in this research project.

Appendix 4 (continued)
Syndromes in Psychiatric Inpatients (Consent Form, Continued)

The nature and possible complications of it have been explained to me.

I also consent that any audio, visual, or psychological test data collected as a result of my participation in this project may be utilized for educational or scientific purposes at Bronx Psychiatric Center or other scientific or educational establishments for a period of time not exceeding indefinite period, after which the data will be erased or destroyed.

I have received assurance that all possible efforts will be made to otherwise preserve my anonimity, privacy, and confidentiality in the use of this material.

I have received assurance that I may withdraw from participation at any time, without affecting my treatment at Bronx Psychiatric Center.

I further understand that my legal rights, regarding negligence and the liability of the institution or its agents, are not waived.

In the case of any physical injury, information on the availability of treatment should be obtained from the Deputy Director, Clinical. Services are available at Bronx Psychiatric Center for immediate medical care and by transfer to Bronx Municipal Hospital Center. Neither the State of New York nor co-sponsors of this study will provide compensation or long-term medical treatment for severe injury or adverse reaction to the procedure.

If I have any questions regarding this research or my rights I may contact the Institutional Review Board Chairperson at 931-0600, extension 2839.

____________________ Name of Person giving information to subject	____________________ Signature of Research Subject
____________________ WITNESSED (other than researcher)	____________________ Date Signed by Subject

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