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PREMORBID ADJUSTMENT AS A PREDICTOR OF SYMPTOM PRESENTATION IN FIRST-EPISODE SCHIZOPHRENIA

By

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ABSTRACT

PREMORBID ADJUSTMENT AS A
PREDICTOR OF SYMPTOM PRESENTATION
IN FIRST-EPISODE SCHIZOPHRENIA

By

Fiona P. Gallacher

The present study sought to further our current knowledge of the clinical course of schizophrenia by providing additional evidence for the existence of phenomenological subtypes, and integrating comprehensive data from two illness epochs that have received considerable attention in recent years, namely, the period before illness onset (premorbid adjustment) and the period during illness onset (first-episode psychosis). Specifically, this study examined the relationships between three patterns of premorbid adjustment (deteriorating, stable-good, stable-poor) and the presence of specific schizophrenic symptomatology (negative symptoms, hallucinations, Schneiderian first-rank symptoms [FRS], thought disorder, bizarre behavior, and paranoia) during first-episode psychosis in order to delineate specific etiologies or developmental pathways of schizophrenia.

An Exploratory Factor Analysis of SANS, SAPS, and BPRS items confirmed the presence of four symptom factors: a negative factor, a "disinhibition" factor (thought disorder and bizarre behavior), a positive factor (hallucinations and Schneiderian FRS), and a paranoid factor. In addition, a Cluster Analysis confirmed the presence of three clusters of patients: a cluster one group with predominantly negative symptoms, a cluster two group with predominantly disinhibition symptoms (thought disorder and bizarre

behavior) and paranoid symptoms, and a cluster three group with predominantly positive symptoms (hallucinations and Schneiderian FRS).

There were significant associations between the deteriorating PMA group and cluster one (negative symptoms); the stable-good PMA group and cluster two (disinhibition and paranoid symptoms) and the stable-poor PMA group and cluster three (positive symptoms). With respect to specific symptomatology the deteriorating PMA group had significantly more negative symptoms than the stable-poor or stable-good group. The stable-good group had more severe paranoid delusions, bizarre behavior, and thought disorder than the deteriorating or stable-poor group, although these differences were not statistically significant. And, the stable-poor group had more severe hallucinations and Schneiderian FRS than the deteriorating or stable-good group, although this difference was not statistically significant.

Overall, these findings provide support for the existence of three developmental pathways of schizophrenia. It appears that patterns in early development are associated with the types of psychotic symptoms one manifests in first-episode psychosis. This information can help to guide us in early detection, prevention, and treatment of first-episode schizophrenia.

To my parents, with love and gratitude.

Patricia Gallacher (1938-1999)

Thomas Gallacher (1936-1984)

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INTRODUCTION AND RATIONALE FOR THE STUDY

Clinical phenomenology has been an area of long-standing interest in the study of schizophrenia. Descriptions of course and outcome in schizophrenia can be found as early as the 1800's when Kraepelin characterized "dementia praecox" as an illness with an early onset, cognitive impairment, and progressive deterioration (Kraepelin, 1896/1987). Later, Bleuler (1911/1950) introduced the term schizophrenia and identified a number of significant clinical features including problems with attention, ambivalence, and affective blunting. Bleuler further proposed that fragmented thinking processes or "associative loosening" constituted a pathognomonic sign of schizophrenia. Psychotic symptoms including hallucinations and delusions have also been characterized as pathognomonic signs of schizophrenia, however, as with thought disorder, have been found in individuals with other illnesses such as bipolar disorder or personality disorders. In a review of the clinical phenomenology of schizophrenia, Andreasen and colleagues (1988) state, "No single symptom can be considered pathognomonic of this disorder. Rather, it is characterized by a polythetic cluster of symptoms, usually expressed in a particular course or pattern" (p. 350). The ability to accurately describe the course or pattern of schizophrenia is essential if predictions regarding etiology and treatment are to be valid.

Crow's (1980, 1985) two-dimensional model has been widely used to describe the clinical course of schizophrenia in the past two decades. This model suggests that there are two syndromes of schizophrenia, namely Type I and Type II. Similarly, Carpenter and colleagues (1988) describe a deficit/non-deficit typology that distinguishes between

proposed "trait" versus "state" characteristics. Many researchers have adopted these two-dimensional models and categorized patients with schizophrenia as either positive or negative based on a number of factors. As outlined by Andreasen and colleagues (1988) positive, Type I, or non-deficit schizophrenia includes factors such as good premorbid adjustment, acute onset, predominant positive symptoms, favorable response to neuroleptic treatment, and neurochemical abnormalities such as hyperdopaminergic transmission. In contrast, negative, Type II, or deficit schizophrenia includes factors such as poor premorbid adjustment, insidious onset, predominant negative symptoms, poor response to neuroleptic treatment, cognitive impairment, and structural brain abnormalities such as ventricular enlargement.

While the advent of factor and cluster analyses further confirmed the positive and negative dimensions of schizophrenia, they also suggested a more complex picture. Specifically, numerous researchers began to describe the presence of a third factor. For example, Strauss, Carpenter, & Bartko (1974) suggested that positive symptoms, negative symptoms, and premorbid social functioning were all independent pathological processes. Other researchers have described a third dimension of schizophrenia called "disorganization." The disorganization or disinhibition factor is primarily characterized by thought disorder, inappropriate affect and bizarre behavior (Arndt, Alliger, & Andreasen, 1991; Gur et al., 1991; Miller, Arndt, & Andreasen, 1993: Peralta, DeLeon, & Cuestra, 1992; Shtasel, Gur, Gallacher, Heimberg, Cannon, & Gur, 1992b; Thompson & Meltzer, 1993). In addition, more complex factor and cluster analyses results have suggested the existence of fourth and fifth factors of schizophrenia (He & Zhang, 2000; Lenzenweger & Dworkin, 1996; Lykouras, Oulis, Daskalopoulou, Psarraos, &

Christodoulou, 2001; Peralta et al., 1992; Shtasel et al., 1992b).

Controversy remains about the existence of "pure" dimensions or developmental and clinical subtypes in schizophrenia. Some researchers have emphasized the heterogeneity of the disorder in their descriptions of the overlap between positive and negative symptoms (Andreasen, Flaum, Swayze, Tyrrell, & Arndt, 1990; Kay, 1991). For example, authors of a review of treatment, services and environmental factors in schizophrenia describe, "Most investigators assume that at least several disease entities will be defined within the schizophrenic syndrome; and that a more definitive nosology for schizophrenia and schizophrenia like psychoses will emerge from further scientific study" (Carpenter et al., 1988, p. 427).

In recent years researchers have attempted to provide a more definitive nosology and comprehensive description of the clinical course of schizophrenia by studying a number of "illness epochs." These illness epochs include all areas of the lifespan, from prenatal and genetics studies (Gottesman, Shields, & Hanson, 1982; Mednick & Cannon, 1991) to post-mortem brain studies (Arnold et al., 1995a). Similarly, some researchers have focused on childhood-onset schizophrenia (Eggers & Bunk, 1997) and others on late-onset schizophrenia or psychosis in geriatric populations (Arnold et al., 1995b; Copeland et al., 1998). Many focus on identifying individuals at high risk for developing schizophrenia (Mednick, Parnas, & Schulsinger, 1987; Olin & Mednick, 1996), while others are concerned with long-term treatment outcome of chronic patients (Szymanski, Cannon, Gallacher, Erwin, & Gur, 1996). Although extensive research exists on discreet illness epochs in the course of schizophrenia, limited attention has been given to systematic integration of this information. Synthesis of comprehensive data across the

lifespan can help provide invaluable information regarding etiology, course, and outcome in schizophrenia.

The present study attempted to further our current knowledge of the clinical course of schizophrenia by integrating comprehensive data from two illness epochs that have received considerable attention in recent years, namely, the period before illness onset (i.e., premorbid adjustment) and the period during illness onset (i.e., first-episode psychosis). Interest in the early course of the disorder continues to grow due to its predictive potential. Specifically, the identification of childhood precursors of adult schizophrenia has expanded our understanding of the etiology of the disorder (Mednick et al., 1987). Similarly, the study of good versus bad premorbid adjustment has begun to provide critical information about possible developmental subtypes of schizophrenia (Andreasen et al., 1988; Crow, 1980) although to date, the data in this area are limited. Most studies that have looked at patterns of premorbid adjustment have divided adjustment into only two categories (i.e., good versus bad) (Harrow, Westermeyer, Silverstein, Strauss, & Cohler, 1986). Similarly, most studies that have attempted to investigate the relationships between patterns of premorbid adjustment and clinical symptomatology have divided symptoms into only two categories (i.e., positive versus negative) (Andreasen et al., 1990). This study aimed to provide a richer, more detailed description of the relationships between patterns of premorbid adjustment and first-episode symptomatology than is currently present in the literature. The identification and description of these relationships sought to provide additional information about specific developmental pathways in the course of the illness.

In addition, focus on early detection and intervention in schizophrenia can lead to less psychological and social disruption and more positive treatment outcomes (Falloon, 1992; Loebel et al., 1992; McGlashan & Johannessen, 1996). As suggested by Harry Stack Sullivan (1953), "many incipient cases might be arrested before the efficient contact with reality is completely suspended" (p. 106) if early detection is prioritized. Therefore, continued investigation of the premorbid and onset phases of schizophrenia appears to be a critical area for further research.

In summary, the proposed research investigated the relationships between specific patterns of adjustment found during the years prior to illness onset (i.e., childhood, early adolescence, late adolescence, and adulthood) and initial symptom presentation during first-episode psychosis. Specifically, this study examined the relationships between three patterns of premorbid adjustment (i.e., deteriorating, stable-good, stable-poor) and the presence of specific schizophrenic symptomatology (i.e., negative symptoms, hallucinations, Schneiderian first-ranked delusions, thought disorder, bizarre behavior, and paranoia/grandiosity) during first-episode psychosis in an attempt to delineate specific developmental pathways of schizophrenia.

LITERATURE REVIEW

Premorbid Adjustment in Schizophrenia

The literature on premorbid adjustment in schizophrenia is vast. The following review will begin with a discussion of the definition of premorbid adjustment, including the time parameters and areas of functioning referred to by the term. It will then provide an overview of common premorbid personality traits found in preschizophrenic individuals. Next, a review of competing theories of premorbid adjustment will be presented. Lastly, an overview of the most contemporary and influential studies to date with respect to premorbid adjustment in schizophrenia in a variety of areas will be provided. These areas include premorbid adjustment in schizophrenia as compared to those with other disorders; correlates of premorbid adjustment in schizophrenia such as demographic variables and biological markers; and premorbid adjustment in schizophrenia and its relationship to subtypes of schizophrenia, clinical symptomatology, treatment outcome and first-episode psychosis.

Definition of Premorbid Adjustment

The term "premorbid adjustment" in relation to schizophrenia refers to the level of adjustment or functioning attained by an individual before the onset of schizophrenia or schizophreniform disorder. Confusion has existed in the literature regarding the precise time period referred to by the term premorbid adjustment. To date it is generally accepted that this period refers to the level of functioning attained at various

developmental stages up to a period of six months before first psychiatric contact or hospitalization. In addition, most definitions of the premorbid adjustment period also state that if psychotic symptoms were present for some time before first psychiatric contact, then ratings should be made of the time period "six months before evidence of characteristic florid psychotic symptomatology including delusions, hallucinations, thought disorder, inappropriate or bizarre behavior, or gross psychomotor behavior in which the symptoms are not apparently due to organic causes" (Cannon-Spoor, Potkin, & Wyatt, 1982, p. 471). Strauss and colleagues (1977) describe premorbid adjustment as "personal functioning measured along various dimensions at specific temporal points" (p. 240). The authors claim that the most important dimensions include functioning in the area of social relations and school or work. Most measures of premorbid adjustment in the literature today assess four areas of functioning. These four areas include sociability-withdrawal, peer relationships including social-sexual relationships, adaptation and performance at work or school, and establishment of independence outside the nuclear family (Cannon-Spoor et al., 1982; Harris, 1975).

Some researchers have distinguished the "prodromal period" from the "premorbid period" in the early course of schizophrenia. Specifically, prodromal symptoms refer to "the early symptoms and signs of an illness that precede the characteristic manifestations of the acute, fully developed illness" (Yung & McGorry, 1996, p. 353). Many investigators describe prodromal symptoms as the first unusual or noticeable behaviors before the development of overt psychotic symptoms (Loebel et al., 1992; Beiser, Erickson, Fleming, & Iacono, 1993). In a comprehensive review of the literature on the prodromal phase of first-episode psychosis, Yung and McGorry (1996) outline the most

commonly described prodromal signs in first-episode studies. These features are shown in Table 1 (see Appendix A). The DSM-III-R (American Psychiatric Association, 1987) included a list of prodromal features of schizophrenia, however, concerns about the reliability and validity of these features led to the list being dropped from DSM-IV (American Psychiatric Association, 1994). According to Keith and Matthew (1991), prodromal symptoms are not included in the ICD-10 (World Health Organization, 1992) because they are too nonspecific and cannot be reliably measured. The risks of confusing "premorbid" and "postmorbid" features in schizophrenia have been discussed repeatedly (Deister & Marneros, 1993; Marneros & Tsuang, 1991; Marneros, Deister, Rohde, Steinmeyer, & Junemann, 1989). Despite continued controversy about the exact characteristics of premorbid and prodromal symptoms in schizophrenia, there does exist general consensus among those who choose to differentiate between premorbid and prodromal phases of schizophrenia regarding the definitions of these chronological periods (McGlashan & Johannessen, 1996). Specifically, the premorbid phase of schizophrenia refers to the time period between birth and first signs of illness. In contrast, the prodromal phase of schizophrenia refers to the time period between the first signs of illness and the onset of psychosis. For the purposes of this study, the premorbid period will refer to the period between birth and six months before first psychiatric contact or hospitalization. Therefore individuals with an insidious onset will likely evidence prodromal features for a significant portion of the premorbid period. In contrast, individuals with a rapid onset will likely not evidence prodromal features at all, or only for a short time during the premorbid period.

Common Premorbid Traits

Although not always the case, observations which date back to Kraepelin (1989/1987) and Bleuler (1911/1950) indicate that some adults with schizophrenia demonstrate unusual behaviors in childhood. Hartmann et al. (1984) report that some studies, "strongly suggest that schizophrenia does not in most cases 'break out' suddenly at the age of twenty years in someone who has had a normal childhood and adolescence" (p. 1055). In contrast, other researchers state, "many individuals who develop schizophrenia have normal childhoods and are not identifiable in their early years" (Torrey, 1995, p. 95).

Despite differences in the presence of premorbid traits in individuals who later develop schizophrenia, there does exist some consensus regarding which traits are most commonly found. For example, Watt and colleagues (1970, 1972, 1978) examined school records of individuals who later developed schizophrenia and found that, in comparison to controls, preschizophrenic boys tended to demonstrate internal conflict, over-inhibition, unsocialized aggression, disagreeable behavior, and emotional depression. In addition, preschizophrenic girls were described as introverted, passive, and emotionally unstable. These authors conclude that between one-third and one-half of preschizophrenic children manifested some type of maladjustment at least a decade before their first hospitalization. A review by Cutting (1985) reported that approximately half of adult schizophrenic subjects evidenced abnormal personality traits in childhood. Examples of these traits include blunted affect, suspiciousness, rigidity, eccentricity, unusual speech, and solitariness (Foerster, Lewis, Owen, & Murray, 1991; Kretschmer, 1921). In a study that retrospectively recalled social functioning in individuals with

schizophrenia and their nonschizophrenic siblings, and normal controls and their well siblings, it was found that the pre-onset childhood and adolescent social functioning of the individuals with schizophrenia was significantly poorer than that of the other three subject groups (Stempel, 1998). In recent years, a number of high risk, longitudinal studies (Erlenmeyer-Kimling, Cornblatt, & Golden, 1983; Goldstein, 1987; Mednick et al., 1987; Tienari et al., 1987) have been developed to look at premorbid behavioral predictors of adult schizophrenia. Many of these studies have demonstrated that individuals who later develop schizophrenia are often withdrawn, anxious, emotionally labile, and at times disruptive (Hans, Marcus, Henson, Auerback, & Mirsky, 1992; John, Mednick, & Schulsinger, 1982; Olin, John, & Mednick, 1995). A similar study that looked at childhood precursors of schizotypal personality disorder (Olin et al., 1997), suggested that those who later developed schizotypal personality disorder were sensitive to criticism, passive, and unengaged in childhood compared to the nonschizophrenic groups. Evidence of behavioral differences between children who later developed schizophrenia and their siblings who did not were found by Walker and Lewine (1990) in a prospective study of children's home movies. Specifically, analysis of these movies demonstrated that the children who later developed schizophrenia were overall less responsive and had poorer fine and gross motor coordination, poorer eye contact, and less positive affect than their siblings who did not develop the disorder. In a prospective, longitudinal study of the children of individuals with schizophrenia, psychiatric controls, and normal controls findings suggest the presence of social impairment and withdrawal in the children of individuals with schizophrenia (Powell, 2000). A study by Hartmann et al. (1984) provides a comprehensive list of psychosocial indicators of vulnerability to

schizophrenia as listed in Table 2 (see Appendix B).

Theories of Premorbid Adjustment

Controversy exists about how early traits or premorbid patterns of adjustment might relate to later symptoms of schizophrenia. Some researchers describe deficiencies in premorbid adjustment as signs of vulnerability to schizophrenia. That is, difficulties in childhood functioning represent early signs of maladjustment, which if not remedied may continue to manifest and worsen over time. Therefore, early traits are the beginnings of a longitudinal process. Researchers have postulated both interpersonal and biological explanations regarding the origins of these early traits. For example, early psychoanalytically oriented theorists emphasized the interpersonal nature of the disorder and suggested that oral dynamics and maternal transference (Bychowski, 1930; Fromm-Reichmann, 1947), poor ego boundaries (Federn, 1943), and poor object relations (Fairbairn, 1954; Freud, 1964; Guntrip, 1969) predispose individuals to the relationship problems indicative of schizophrenia. Melanie Klein (1930, 1948, 1975) furthered the development of a psychoanalytic theory of schizophrenic symptomatology in her work with psychotic patients around early oral dynamics and internalized object relations. In general, Kleinian analysts understand the symptoms of schizophrenia as defenses against terrifying persecutory and annihilation anxieties (Bion, 1967; Rosenfeld, 1969; Segal, 1973). Similarly, Kretschmer (1921) viewed psychotic symptoms as reactions to stress in particularly vulnerable individuals. Sullivan (1953) and Winnicott (1965) also emphasized the interpersonal nature of the disorder, and the influence of environmental deficiencies in the maturational processes of early childhood in individuals who later

develop schizophrenia. Several contemporary psychoanalytically oriented researchers also agree that the symptoms of schizophrenia represent attempts to cope with overwhelming feelings of terror due to traumatic life histories (Karon, 1992; Karon & Teixeira, 1995; Karon & VandenBos, 1981; Teixeira, 1984). In addition, many of the early symptoms present in children who later develop schizophrenia are seen in children who later develop other disorders (e.g. bipolar affective disorder, personality disorders), therefore these traits are seen as not specific to schizophrenia, but instead constitute symptoms on a continuum, with schizophrenia being the most severe (Teixeira, 1998).

In contrast, other researchers would agree with Kraepelin's (1989/1987) view that abnormal personality traits in childhood constitute the early stages or precursors of a longitudinal disease process of abnormal perceptions and relations. Advocates of this viewpoint stress the neurobiological underpinnings of schizophrenia, and therefore see early traits and poor premorbid adjustment as the beginning signs of brain dysfunction or aberrant neurological development (Torrey, 1995; Weinberger, 1995).

Still other researchers focus on describing the deficiencies in premorbid adjustment as leading to increased difficulty in recovering from schizophrenia when it hits. For example, numerous studies stress that poor premorbid functioning, especially social functioning, lead to poor outcome in schizophrenia (Kokes, Strauss & Klorman, 1977; Bailer, Brauer & Rey, 1996). These researchers emphasize that particular premorbid characteristics are not necessarily early signs of schizophrenia, but instead may make it more difficult for the individual who later develops the disorder to cope with the subsequent symptoms.

Premorbid Adjustment in Schizophrenia versus Normal Controls and Other Disorders

Numerous studies have demonstrated that individuals with schizophrenia consistently show poorer premorbid adjustment than normal controls (Cannon-Spoor et al., 1982; Lewine, Watt, Prentky, & Fryer, 1980; Watt, Stolorow, Ludensky, & McClelland, 1970). Krauss and colleagues (1998) found that individuals with schizophrenia or schizoaffective disorder and normal controls differed significantly on every item of the Premorbid Adjustment Scale (PAS; Cannon-Spoor et al., 1982). Many researchers have also shown that individuals with schizophrenia show poorer premorbid adjustment than those with affective disorders (Bromet et al., 1996; Dalkin, Murphy, Glasebrook, Medley & Harrison, 1994; Gureji, Aderibigbe, Olley, & Bamidele, 1994; Maneros et al., 1989; Van Os et al., 1995; Vocisano, Klein, Keefe, Dienst, & Kincaid, 1996). For example, a recent study by Cannon and colleagues (1997) demonstrated that individuals with schizophrenia were impaired in childhood and adolescence both socially and scholastically in comparison to normal controls and individuals with bipolar disorder. In addition, the children who later developed bipolar disorder functioned well scholastically, and were socially impaired only in adolescence, but to a lesser degree than the children who later developed schizophrenia. Of note, the researchers controlled for confounding factors such as sex, social class, ethnicity, and premorbid IQ.

Premorbid Adjustment and Demographic Variables

It has been well established that poor premorbid adjustment in schizophrenia is associated with demographic variables such as male gender and earlier onset of the disorder (Goldstein, Tsuang, & Faraone, 1989; Klorman, Strauss, & Kokes, 1977;

Lewine, 1981; Loranger, 1984; Shtasel, Gur, Gallacher, Heimberg, & Gur, 1992a; Westermeyer & Harrow, 1984). Larsen and colleagues (1996b) found that gender differences during the onset of schizophrenia can be striking, with males evidencing poorer premorbid adjustment than females. The authors further described males' tendency to deteriorate faster than females, especially close to onset of the disorder. Some researchers suggest that these differences may be due to males' higher incidence of brain insult in childhood (Nasrallah & Wilcox, 1989) or brain morphology (Lewine, Gulley, Risch, Jewart, & Houpt, 1990). It has also been suggested that womens' later onset and less severe course may be due to the "protective effect" of estrogen (Hafner et al., 1998; Seeman & Lang, 1990; Woolley & McEwen, 1994). Others have hypothesized that differences in the expression of schizophrenia may be a result of cultural and social factors (Loranger, 1984), such as sex differences in depth of affect (Shtasel et al., 1992a).

Premorbid Adjustment and Biological Markers

Studies examining the relationship between poor premorbid adjustment and biological markers suggest that difficult premorbid functioning is associated with neurological impairment (Guy, Liaboe, & Wallace, 1986; Lilliston, 1970), minor physical anomalies which have been hypothesized to originate from first trimester trauma (Guy, Majovski, Wallace, & Guy, 1983), impaired N2 auditory event-related potential (Levitt, O'Donnell, McCarley, Nestor, & Shenton, 1996), CT scan abnormalities (Weinberger, Cannon-Spoor, Potkin & Wyatt, 1980), enlarged ventricles (Levitt, Shenton, McCarley, Faux, & Ludwig, 1994; Weinberger et al., 1980), and temporal lobe impairment (Saykin et al., 1991). Poor premorbid adjustment has also been associated with

neuropsychological deficits including impaired performance on the visual memory span task of the Wechsler Memory Scale and more perseverative errors on the Wisconsin Card Sorting Test (Levitt et al., 1996).

Premorbid Adjustment and Subtypes

Interest in investigating the temporal features of onset in schizophrenia has been generated by a desire to identify both developmental and clinical subtypes of the disorder (Bleuler, 1978; Ciompi, 1980). To this end, numerous investigations of the relationship between premorbid adjustment and the various subtypes of schizophrenia have been conducted. Many researchers in the area of premorbid adjustment have emphasized the paranoid versus non-paranoid subtype distinction. Despite some evidence which supports no differences (Eisenthal et al., 1972; Sanes & Zigler, 1971), it is now generally accepted that individuals who have paranoid schizophrenia have a better premorbid adjustment than those who have disorganized or undifferentiated types of schizophrenia (Deister & Marneros, 1993; Magaro, 1981; Zigler, Levine, & Zigler, 1977). Deister and Marneros (1993) reported that significantly more patients with paranoid initial episodes had a stable social-sexual partnership before onset than patients with residual, negative or catatonic subtypes. Similarly, the lowest rates of social isolation were found among the patients with paranoid in comparison to disorganized subtypes. Lastly, a study of premorbid functioning in a sample of state hospital patients found that paranoids had higher levels of social competence than non-paranoids (Zigler & Levine, 1973).

Premorbid Adjustment and Negative Symptoms

Considerable evidence indicates a relationship between poor premorbid adjustment and negative symptomatology (Andreasen & Olsen, 1982; Andreasen et al., 1990; Dworkin et al., 1987; Kay & Lindenmayer, 1987; Pogue-Geile & Harrow, 1984). Specifically, McGlashan and Fenton (1992) reported that poor premorbid functioning in the areas of social relationships, educational attainment, and work performance are all associated with the development of the negative symptoms of schizophrenia (i.e., affective flattening or blunting, alogia, avolition-apathy, anhedonia-asociality and attention). Peralta and colleagues (1991) investigated the relationship between negative symptoms and presence of premorbid personality disorders and reported that affective flattening and alogia were more frequently present and severe in schizophrenics who met criteria for schizoid or schizotypal personality disorder before onset of schizophrenia than those who did not. In addition, some studies have demonstrated that the relationship between poor premorbid adjustment and negative symptoms is stronger in men than women (Ring et al., 1991, Shtasel et al., 1992a). Studies examining first-episode populations have further demonstrated that the relationship between poor premorbid adjustment and negative symptomatology holds across a wide range of methodologies and age ranges (Dalkin et al., 1994; Haas & Sweeney, 1992; Larsen, McGlashan, & Moe, 1996a; Larsen, McGlashan, Johannessen, & Vibe-Hansen, 1996b; Larsen, Moe, Vibe-Hansen, & Johannessen, 2000; Peralta, Cuestra, & DeLeon, 1991; Shtasel et al., 1992b).

Premorbid Adjustment and Treatment Outcome

There is substantial evidence to indicate that poor premorbid adjustment is also associated with unfavorable treatment outcomes in schizophrenia (Fenton & McGlashan, 1987; Kay & Lindenmayer, 1987; Larsen et al., 2000; McGlashan, 1986; Prudo & Blum, 1987; Strauss & Carpenter, 1974). Numerous studies have demonstrated that poor premorbid adjustment is associated with slower remission of symptoms and less improvement in community adjustment over time (Bromet et al., 1996; Gittelman-Klein & Klein, 1969; Strauss & Carpenter, 1977). Poor premorbid adjustment has also been associated with poor response to neuroleptic medication (Goldstein, 1970; Stern et al., 1993; Sternberg, van Kammen, Lerner & Bunney, 1982). A retrospective case study by Amminger and Mutschlenchner (1995) demonstrated that patients who showed complete remission after eight weeks of neuroleptic medication had significantly higher social functioning ratings during childhood than patients who showed only a partial remission or no response. Wieselgren and Lindstroms' (1996) data suggest that schizophrenics who evidence deviant premorbid behavior, such as problems in school with friends or teachers are more likely to have a poor outcome than those who show no deviant behavior. Overall, various researchers have indicated that when looking at a number of potential predictive variables in schizophrenia, premorbid adjustment is the strongest overall predictor of outcome (Bailer, Brauer, & Rey, 1996; Bromet et al., 1996; Strauss & Carpenter, 1977).

Patterns of Premorbid Adjustment

The majority of early studies of premorbid adjustment in schizophrenia used a simple, two-dimensional design and categorized individuals as having either good or poor premorbid adjustment. This two-dimensional model was expanded (Bromet, Harrow, & Kasl, 1974; Chapman et al., 1961; Vaillant, 1964) when good premorbid adjustment was associated with a reactive-type psychosis and poor premorbid adjustment was associated with a process-type psychosis. As outlined by Heilbrun, Blum, & Goldreyer (1985), "Reactive schizophrenics, by definition, are more responsive to their social environment than process schizophrenics. The major factors in the better premorbid adjustment of the reactive are greater commitment to, and success in, social relationships and greater commitment to attainment of socially recognized goals" (p. 105). One of the most widely used measures of premorbid adjustment, namely the Phillips Scale (Phillips, 1953), has often been used to classify individuals with schizophrenia as process or reactive based on their ratings of premorbid social and sexual adjustment. According to Harrow and colleagues (1986, p. 195), "Literally thousands of studies have been based on the process-reactive dimension and on good versus poor premorbid social adjustment -- two related but not necessarily identical concepts" (Bromet et al., 1974; Chapman & Chapman, 1973; Putterman & Pollak, 1976; Strauss & Carpenter, 1974; Quitkin, Rifkin & Klein, 1976).

The methodological flaws inherent in classifying subjects into dichotomies such as good versus bad premorbid adjustment have been outlined (Sorensen, Paul, & Mariotto, 1988). Zigler, Levine and Zigler (1977) suggest that such dichotomies artificially constrict the true variance that exists in premorbid functioning. Instead they

suggest that better characterization of premorbid adjustment can be achieved by measuring multiple levels of functioning. Examining the mode of onset (i.e. gradual versus sudden) may increase understanding of the course of schizophrenia (Carpenter & Kirkpatrick, 1988; McGlashan, 1988). For example, recent studies have characterized premorbid functioning based on three subtypes: stable-poor, deteriorating, and stable-good (Haas & Sweeney, 1992; Larsen et al., 1996b). Specifically, the stable-poor group refers to individuals who show consistently low levels of functioning from childhood through adolescence and adulthood. The deteriorating group refers to individuals who evidence a pattern of progressive or insidious decline in functioning from childhood through adolescence and adulthood. And the stable-good group refers to individuals who show consistently adequate to good levels of functioning from childhood until the onset of first psychotic symptoms.

Results of these studies indicate that individuals with a deteriorating course of premorbid functioning evidence more severe negative symptoms (i.e., anhedonia and social withdrawal) than both the stable-good and the stable-poor groups (Haas & Sweeney, 1992; Larsen et al., 1996b). In addition, the stable-good group showed both a later age of symptom onset as well as a later age of first psychiatric contact. This finding is consistent with previous data which suggest that later age of onset and good premorbid functioning are associated with a more benign course of illness (World Health Organization, 1979; Burack & Zigler, 1989).

Patterns of Clinical Symptoms

A number of standardized clinical rating scales have been developed in the past two decades to assess the presence and severity of symptomatology in schizophrenia. Hughlings-Jackson was the first to use the terms positive and negative with respect to symptomatology in the context of a model of brain function (Hughlings-Jackson, 1931). Negative symptoms involved a loss of function through damage to some area of the brain, whereas positive symptoms involved a release of function by damage to the higher cortical area that worked to inhibit the function. Hughlings-Jackson later described positive and negative psychiatric symptoms. He concluded that affective flattening or alogia were caused by loss of function, and therefore negative symptoms and hallucinations and delusions were caused by a release of function and therefore positive symptoms. Crow (1980) and Andreasen and Olson (1982) extended the ideas of Hughlings-Jackson and further differentiate between the 'positive' and 'negative' symptoms of schizophrenia. As outlined by Carpenter et al. (1988), "While the positive symptoms represent an exaggeration or distortion of normal function (i.e., hearing voices when none are there), negative symptoms represent a diminution or loss of normal functioning" (p. 350). This differentiation lead to the creation of standardized rating scales such as the Scale for the Assessment of Positive Symptoms (SAPS) and the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1982, 1983, 1984). The Scale for the Assessment of Positive Symptoms (SAPS) includes ratings of the most striking psychotic symptoms of schizophrenia such as auditory and visual hallucinations, paranoid and grandiose delusions, positive formal thought disorder and bizarre behavior.

In contrast, the Scale for the Assessment of Negative Symptoms (SANS) includes ratings of affective flattening or blunting, alogia, avolition-apathy, anhedonia-asociality and attention. Another clinical rating scale that has held broad appeal in the research community is the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962). This scale includes a broad range of symptoms and assesses many of the symptoms of schizophrenia in a general way. For example, the BPRS includes a global rating of hallucinatory behavior, as opposed to detailed ratings of auditory, somatic, olfactory and visual hallucinations found on the SAPS.

It has been suggested that about one-third of patients with schizophrenia have predominantly positive symptoms, one-third have primarily negative symptoms, and one third have a mixed symptom presentation of both positive and negative symptoms (Andreasen & Olsen, 1982). Factor analysis of the SAPS and SANS has confirmed the positive-negative dimensions of schizophrenia and suggested the presence of a third "disorganization" factor (Arnt et al., 1991; Miller et al., 1993; Peralta et al., 1992). This disorganization or disinhibition factor consists primarily of symptoms of thought disorder, as well as extravagant, bizarre or inappropriate behavior and affect. Factor analysis of the BPRS has indicated five factors, namely anxiety-depression, anergia, thought disorder, activity, and hostility (Guy, Cleary & Bonota, 1975). Gur, Resnick and Gur (1989) repeated this factor analysis of BPRS items, but divided them into symptoms specific to schizophrenia (e.g., suspiciousness, hallucinatory behavior, unusual thought content) and those non-specific to schizophrenia (e.g., anxiety, guilt feelings, depressive mood). The results of this analysis suggested that patients with schizophrenia scored higher on specific symptoms than depressed patients and that there was a correlation

between severity of specific symptoms and regional cerebral blood flow and glucose metabolism.

In another study of the relations among clinical scales Gur and colleagues (1991) compared specific and nonspecific ratings on the BPRS, global ratings on the SAPS and SANS, and deficit/non-deficit ratings (Carpenter, Heinrichs, & Wagman, 1988) in a sample of patients with schizophrenia. Because the BPRS includes psychiatric symptoms that are both specific to schizophrenia (e.g., conceptual disorganization, hallucinatory behavior, unusual thought content, blunted affect) and nonspecific to schizophrenia (e.g., anxiety, guilt feelings, depressive mood, uncooperativeness) it makes clinical sense to divide the items in this way. Carpenter developed the deficit/non-deficit scale to distinguish between long-standing negative symptoms of schizophrenia (deficit) and transitory negative symptoms that might be caused by secondary factors (non-deficit). Gur et al. (1991) reported that deficit patients had more specific symptoms, fewer nonspecific symptoms, and more negative symptoms. In addition, results of a cluster analysis suggested three clusters of patients. The first cluster consisted of primarily non-deficit patients who had high specific symptoms and low nonspecific symptoms. The second cluster consisted of primarily deficit patients with high scores on specific symptoms, positive and negative symptoms. And the third cluster consisted of primarily deficit patients with low scores on specific symptoms, and high scores on positive and negative symptoms.

A similar study by Shtasel and colleagues (1992b) compared first-episode with non first-episode patients and extended their factor analysis to include all items on the SAPS, SANS, and BPRS. Results from this analysis yielded a four-factor solution. The

first factor included symptoms associated with the negative or deficit syndrome. The second factor included disorganization or disinhibition symptoms such as positive formal thought disorder and bizarre behavior. The third factor included hallucinations and Schneiderian first-rank symptoms (FRS) (e.g., mind reading, thought insertion and withdrawal) (Schneider, 1959). The fourth factor included paranoia and grandiosity. A cluster analysis was then done on the four factors (i.e., negative symptoms, thought disorder/bizarre behavior, hallucination and Schneiderian FRS, and paranoia/grandiosity). This analysis produced three clusters of patients. The first cluster represented a group of patients with severe negative symptoms and moderate thought disorder, delusions and hallucinations. The second cluster represented a group of patients with predominantly thought disorder/bizarre behavior, and paranoia/grandiosity. And the third cluster of patients included those with severe hallucinations and Schneiderian FRS. One of the most notable findings in this study was the lack of difference between first-episode and non first-episode patients in overall severity of symptoms. Some differences were found on specific symptoms. For example, first-episode patients had less severe ratings with respect to thought disorder and more severe ratings with respect to delusions and hostility. The two groups did not differ in negative symptomatology. Further analysis suggested that poor premorbid and current functioning are associated with negative symptoms in both first-episode and non-first-episode groups.

Benefits of First-Episode Populations

The benefits of studying first-episode populations have been described by numerous researchers (Keshavan & Schooler, 1992; Lieberman, Matthews, & Kirch, 1992; Shtasel et al., 1992b). Some emphasize that a detailed analysis of the time period surrounding first-episode psychosis is critical for an accurate picture of schizophrenia because the majority of clinical changes occur early on in the disorder (Bilder et al., 1992; Lieberman et al., 1992). Haas and Sweeney (1992) indicate, "One of the chief advantages is that the clinical symptomatology and behavior observed during the first episode are less affected by the confounding influences of medical treatments, secondary social difficulties, and disease progression" (p. 374). The presence of confounding variables such as the use of neuroleptic medication, stigma, long-term treatment in the community, and repeated hospitalizations are likely with a chronic schizophrenic population. Issues regarding increased reliability of data are also an important benefit of studying first-episode populations. Specifically, the relatively short time span between the onset of symptoms and clinical documentation enhances accuracy of recall for both the patient and any third-party reporters such as family members (Haas & Sweeney, 1992).

Issues regarding the definition of first-episode schizophrenia have been discussed at length in the literature. Flaum and colleagues (1992) point out the often elusive nature of schizophrenia onset. They discuss the importance of an operationalized definition of first-episode because "patients who experience a chronic and unremitting course could be said to be in their first episode for most of their lives" (p. 482). For the purpose of this

study first-episode was defined as the first time psychiatric treatment was sought and accepted by neuroleptic naive patients who receive a diagnosis of schizophreniform disorder or schizophrenia.

THE PRESENT STUDY

Overview

Schizophrenia is seen as the most severe form of mental illness because those who suffer from it have broken ties with reality. This break with reality can manifest itself in various ways and to various degrees. In general, it makes sense that the longer an individual has been engaged in breaking ties with reality, the more severe his or her psychotic symptoms. From this theoretical perspective, we are not seeing differential disease processes in the various manifestations of schizophrenia, but instead one disease process that falls on a continuum of severity. For example, negative symptoms can be seen as a less severe form of psychosis, because the individual has simply withdrawn from reality, not created alternative realities in the form of hallucinations and delusions. Similarly, thought disorder and paranoia can be seen as less severe forms of psychosis in comparison to hallucinations and delusions because of their interpersonal nature. That is, the individual with thought disorder has developed faulty communication patterns and the paranoid individual has developed a faulty connection with others. Overall, this theoretical perspective points to the existence of complex relationships between patterns of premorbid functioning and the development of various types of schizophrenic symptomatology.

The current study aimed to extend the work on premorbid functioning and symptomatology in schizophrenia by attempting to further determine the relationship between patterns of premorbid adjustment and specific symptom presentation in first-

episode schizophrenia. Specifically, the aim of the current research was to further assess the association between patterns of premorbid adjustment based on Haas and Sweeney's (1992) subtypes (i.e., stable-poor, deteriorating, and stable-good) and the four symptom factors (i.e., negative, disinhibition, positive, paranoia) and three patient clusters (i.e., a predominantly "negative" group with moderate delusions, hallucinations and thought disorder; a predominantly "disinhibited" group with moderate thought disorder, bizarre behavior, and paranoia; and a predominantly "positive" group with severe hallucinations and Schneiderian FRS) described by Shtasel et al. (1992b).

First, previous research suggests that the deteriorating premorbid group will evidence more negative symptomatology than the stable-good and stable-poor groups (Haas & Sweeney, 1992; Larsen et al., 1996b). Next, it is indicated that paranoid schizophrenia is directly related to good premorbid adjustment (Ritzler, 1981; Zigler & Levine, 1973), therefore, it is expected that the stable-good group will evidence more paranoid and grandiose symptomatology than the stable-poor or deteriorating group. Lastly, a recent study by Bailer and colleagues (1996) suggested that the highest proportion of positive symptoms (e.g. hallucinations, delusions) was found in the poor premorbid adjustment group as compared to the good, therefore it is expected that the stable-poor group will evidence more hallucinations and Schneiderian first-ranked symptoms than the stable-good or deteriorating group.

Research Hypotheses

The present study addressed the following hypotheses:

1. It was predicted that an Exploratory Factor Analysis of all SANS, SAPS, and BPRS items would evidence the same four-symptom factor solution as previously determined in the Shtasel et al. (1992b) study. Specifically, it was predicted that the four factors would include, 1) a negative factor, 2) a thought disorder/bizarre behavior factor, 3) a hallucinations/Schneiderian FRS factor, and 4) a paranoid/grandiose factor.

2. It was predicated that a Cluster Analysis of the four symptom factors would produce three clusters of patients as previously determined in the Shtasel et al. (1992b) study. Specifically, it was predicted that:

   a) Cluster 1 would represent a group of patients with prominent negative symptoms.

   b) Cluster 2 would represent a group of patients with prominent paranoia/grandiosity and thought disorder/bizarre behavior.

   c) Cluster 3 would represent a group of patients with prominent hallucinations and Schneiderian FRS.

3. It was predicated that the three clusters of patients would evidence significantly different patterns of premorbid adjustment. It was further predicated that:

   a) Cluster 1 would evidence a deteriorating pattern of premorbid adjustment.

b) Cluster 2 would evidence a stable-good pattern of premorbid adjustment.

c) Cluster 3 would evidence a stable-poor pattern of premorbid adjustment.

4. With respect to specific symptomatology it was predicted that:

a) The deteriorating group would evidence the most severe negative symptoms, in comparison to the stable-poor or stable-good group.

b) The stable-good group would evidence the most severe paranoid delusions, bizarre behavior and thought disorder in comparison to the deteriorating or stable-poor group.

c) The stable-poor group would evidence the most severe hallucinations and Schneiderian FRS in comparison to the deteriorating or stable-good group.

METHODOLOGY

Subjects

Subjects included eighty-six adults with a diagnosis of first-episode schizophrenia, schizoaffective disorder, or schizophreniform disorder. Subjects were categorized as first-episode because they were experiencing psychotic symptoms for the first time, had not accepted psychiatric treatment in the past, and were neuroleptic naïve. Subjects were recruited by the University of Pennsylvania's Neurobehavioral Study of Schizophrenia research team and were selected from an ongoing longitudinal study investigating brain function in schizophrenia. Subjects were referred from private practitioners, community mental health centers, emergency rooms, state hospitals, and the inpatient unit of the Hospital of the University of Pennsylvania. Subjects were excluded from the study if they had: 1) a concomitant axis I or II psychiatric disorder; 2) past or present substance abuse or dependence; 3) a history of a medical illness that might effect brain function (e.g., cardiac, endocrine, pulmonary, or renal disease); 4) a history of a neurological disorder (e.g.,. epilepsy, migraines, head trauma with loss of consciousness); 5) current pregnancy.

Clinical Assessment

After informed consent was obtained, subjects underwent a comprehensive intake evaluation as part of enrollment into the University of Pennsylvania's Neurobehavioral

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Study of Schizophrenia. Intake evaluations were conducted by members of the research team and included both medical and psychiatric components. The medical component included a history, physical examination, and routine laboratory tests. None of the medical data were used in the present study. The psychiatric component included a standard clinical interview (SCID-P; Spitzer, Williams, Gibbon, & First, 1989, 1994) and personality questionnaires. Diagnoses were based on information gained from the standard clinical interview, chart review, and discussions with family members and other professionals (e.g. inpatient unit or emergency room staff). After an interview, the interviewer completed numerous clinical rating scales that characterized premorbid adjustment, symptom presentation, and social and occupational functioning. The following clinical rating scales were used in the present study: the Premorbid Adjustment Scale (PAS; Cannon-Spoor et al., 1982), the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1982, 1983), the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984), and the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962). Other rating scales and personality questionnaires were completed but were not used in the present study. Psychiatric interviews and rating scales were completed by members of the research team trained to a criterion reliability of a minimum of 0.90 intraclass correlation on each instrument. Intake evaluations were performed at the Hospital of the University of Pennsylvania. All subjects were interviewed while off neuroleptic medications and clinical rating scales were completed within 5 days of study entry.

Measures

The Premorbid Adjustment Scale

Most rating scales used to measure premorbid adjustment in schizophrenia were developed thirty years ago. Examples of these scales include the Elgin Prognostic Scale (Wittman, 1941), the Phillips Scale (Phillips, 1953), and The Premorbid Asocial Adjustment Scale (Gittelman-Klein & Klein, 1969). Cannon-Spoor and colleagues (1982) developed the Premorbid Adjustment Scale (PAS) in an attempt to remedy some of the limitations of using outdated instruments. For example, many of the anchor points on the old scales no longer reflected cultural norms. Also, none of the old scales evaluated premorbid adjustment systematically at several developmental time points. The authors reported that the PAS, "1) was useful for research purposes, 2) conceptualized successful premorbid adjustment in terms of the attainment of certain developmental goals that were viewed as necessary milestones for healthy functioning, and 3) considered attainment of these goals as specific age-related tasks" (p. 471).

The PAS is designed to evaluate level of functioning in four major areas. These areas include social accessibility-isolation, peer relationships, ability to function outside the nuclear family, and capacity to form intimate social-sexual ties. Items that evaluate age-appropriate functioning in each of these areas are included for Childhood (birth up to age 11), Early Adolescence (age 12-15), Late Adolescence (age 16-18), and Adulthood (19 years and beyond). The final section is labeled General, and contains items to assess the highest level of functioning attained before the individual became ill, the time span and characteristics of illness onset, and general information including education and

establishment of independence. There are a total of 23 items on the PAS.

Ratings were based on interviews with patients and as many sources of corroborating information as possible. Family member reports, school and hospital records, and information from other professionals such as teachers or physicians often augment the information provided in a personal interview. Each item was rated based on a 0-6 Likert type scale, with 0 representing the healthiest end of the adjustment range, and 6 representing the least healthy. All items included descriptive anchor points to increase reliability and validity.

Cannon-Spoor and colleagues (1982) describe two studies of PAS interrater reliability. In the first study, two raters who were familiar with the PAS rated 11 patients. Both raters reviewed chart notes and in some cases interviewed patients simultaneously. Each rater completed the PAS independently. The intraclass correlation coefficient was $r = .85$ ($p = .0001$). In the second study, ratings of three Veteran's Administration hospital (VA) clinicians and two National Institute of Mental Health (NIMH) clinicians unfamiliar with the PAS were compared. All five clinicians reviewed chart notes only. The average intraclass correlation coefficient was $r = .74$ ($p = .0001$).

Cannon-Spoor et al. (1982) have addressed issues of validity by comparing the PAS ratings of subjects with schizophrenia to normal populations, and outpatients to chronically hospitalized patients. In a study that compared 76 normal controls and 86 patients with schizophrenia, the normal group was significantly different ($p < .01$, two-tailed *t* test) on every subscale as well as on overall average score than the schizophrenic group. Similarly, when the PAS scores of current outpatients were compared to those of patients who had been continuously hospitalized for the past seven years, significant

differences were found between the groups. These discriminations were found on all subscales except Childhood (Early Adolescence, p = .02; Late Adolescence, p = 009; Adulthood, p = .02; and Average score, p = .002; one-way analysis of variance).

Krauss and colleagues' (1998) report on the reliability and validity of the PAS in a study of 86 German patients with schizophrenia and schizoaffective disorder and 38 normal controls. In this sample, the estimation of the reliability coefficients showed high positive values of Cronbach's alpha between .80 and .93. In addition, the researchers reported that patients and normal controls significantly differed on all items of the PAS.

For the purposes of the current study, premorbid functioning was classified based on PAS scores, into one of three patterns of premorbid adjustment, as identified by Haas & Sweeney (1992): 1) deteriorating or insidious premorbid functioning before onset of first psychotic symptoms; 2) stable-good premorbid adjustment, identified by consistently adequate-to-good levels of premorbid functioning from childhood until onset of first psychotic symptoms; and 3) stable-poor premorbid adjustment, identified by consistency low levels of functioning from childhood until time of onset of first psychotic symptoms. For the purpose of consistency, the definitions and cut-offs used by Haas & Sweeney (1992) and Larsen et al. (1996) were implemented. The deteriorating group was defined with a pattern of worsening scores from childhood throughout the various developmental periods and "the equivalent of a two-point change over four premorbid stages (childhood, early adolescence, late adolescence, and adulthood) or a proportionate decline for cases in which illness onset was before late adolescence or adulthood" (Haas & Sweeney, 1992, p. 376). In other words, the average score for each developmental period was calculated, and an individual was categorized as deteriorating if their scores dropped by two points,

between childhood and adulthood. In contrast to the deteriorating group, the good and poor groups were defined with a stable pattern of adjustment across premorbid periods. All subjects who did not meet criteria for the deteriorating group were placed in the stable-good or stable-poor group based on their overall mean PAS score. The overall mean PAS score was used as a cut-off point to divide the cases into stable-good or stable-poor.

The Scale for the Assessment of Negative Symptoms

In recent years the importance of distinguishing between positive and negative symptoms in schizophrenia has been widely accepted (Crow, 1980; Strauss et al., 1974). Andreasen (1982, 1983) was the first to develop a standardized method to define and rate negative symptoms in schizophrenia with the creation of the Scale for the Assessment of Negative Symptoms (SANS). The SANS contains items for rating 24 negative symptoms, including 5 global symptoms. Andreasen included the following global symptoms (i.e., alogia, affective flattening, avolition-apathy, anhedonia-asociality, and attentional impairments) which "were chosen empirically, based on [her] 12 years experience evaluating, treating, and following many schizophrenic patients in a single setting" (p. 785). Each of the five global areas is broken down into observable behavioral components that are rated on a 6-point Likert scale ranging from (0) None to (5) Severe. For example, the global symptom of avolition-apathy refers to an overall lack of energy, drive, and interest. The patient is rated globally, as well as on the specific items of grooming and hygiene, impersistence at work or school, and physical anergia. A total score of all items is calculated to give the rater a sense of overall severity of pathology.

Andreasen (1982) originally reported the reliability of the SANS using only an interrater reliability design. This approach was chosen over a test-retest design because the primary goal was to determine how well two independent raters would agree on ratings of various patient behaviors. Also the use of the test-retest design introduces an additional source of variance (i.e., changes in the patient's behavior over time). Andreasen (1982) reported intraclass reliability scores that include both individual items as well as global scores. The global intraclass reliability scores are as follows: anhedonia, $r = 0.81$; affective blunting, $r = 0.80$; avolition, $r = 0.86$; alogia, $r = 0.66$; and attention, $r = 0.67$. Consistently high reliability scores have been reported in a number of studies from Japan, Spain, and Italy (Humbert, Salvador, Segui, Obiols, & Obiols, 1986; Moscarelli, Maffei, & Cesana, 1987; Ohta, Okazaki, & Anzai, 1984). Examples of these intraclass reliabilities include ranges of $r = 0.75$ to $r = 0.86$ for affective flattening and $r = 0.73$ to $r = 0.86$ for anhedonia-asociality.

Later, Andreasen (1990) added to her work by reporting SANS test-retest reliability scores. For this study, two clinicians simultaneously evaluated a patient on two consecutive days in order to ensure minimal change in symptoms over time. Test-retest reliability scores were somewhat poorer than interrater reliability scores, but most global ratings continued to be in the acceptable range. Global test-retest reliability scores include the following: anhedonia, $r = 0.71$; affective blunting, 0.76; avolition, 0.67; alogia, 0.38; attention, 0.46.

Andreasen (1990) reported the reliability coefficient of each global symptom on the SANS using Cronbach's alpha. This coefficient measures the extent to which all items in a given subscale measure the same symptom complex. Cronbach's alpha is

adequate for all 5 global symptoms: affective flattening (0.83), alogia (0.63), attentional impairment (0.75), avolition-apathy (0.74), and anhedonia-asociality (0.77). Cronbach's alpha was also determined for the composite score (the sum of all items) as 0.89. As described by Andreasen (1990), the high scores suggest that the items on the negative symptom scale are highly integrated to one another.

The Scale for the Assessment of Positive Symptoms

Shortly after the development of the SANS to rate negative symptoms of schizophrenia, Andreasen (1984) decided to create a similar standardized method to define and rate positive symptoms of schizophrenia. This instrument is called The Scale for the Assessment of Positive Symptoms (SAPS). The SAPS contains items for rating 34 positive symptoms, including 4 global symptoms. Andreasen included the following global symptoms (i.e., hallucinations, delusions, bizarre behavior, and positive formal thought disorder). As with the SANS, each of the global areas is broken down into observable behavioral components that are rated on a 6 point Likert scale ranging from (0) None to (5) Severe. For example, the global symptom of hallucinations is based on the duration and severity of the hallucinations and their effects on the patient's life. The patient is rated globally, as well as on the specific items of auditory hallucinations, voices commenting, voices conversing, somatic or tactile hallucinations, and visual hallucinations. A total score of all items is calculated to give the rater a sense of overall severity of pathology.

Andreasen (1990) reported SAPS intraclass reliabilities for individual items as well as the global scores. The global intraclass reliabilities are as follows: hallucinations,

r = .0.93; delusions, r = 0.76; bizarre behavior, r = 0.62; and, positive formal thought disorder, r = 0.79. As with the SANS, the interrater reliabilties of the SAPS are consistently high across a wide range of cultural settings. Studies which compared multiple raters in Italy, Spain, and Japan reported global ratings of hallucinations ranging from intraclass r = 0.84 to r = 0.93. Similarly, global ratings of positive formal thought disorder were reported ranging from intraclass r = 0.82 to r = 0.99. According to Andreasen (1990), such high interrater reliabilities suggest "the soundness of the basic strategy of using observational rather than subjective evaluation" (p. 80).

Later, Andreasen (1990) added to her work by reporting SAPS test-retest reliability scores. For this study, two clinicians simultaneously evaluated a patient on two consecutive days in order to ensure minimal change in symptoms over time. Test-retest reliability scores were somewhat poorer than interrater reliability scores, but most global ratings continued to be acceptable. Global test-retest reliability scores include the following: hallucinations, r = 0.65; delusions, r = 0.71; bizarre behavior, 0.50; positive formal thought disorder, r = 0.62. As outlined by Andreasen (1990), test-retest reliability includes components of both rater variance (differences in raters over time) as well as occasion variance (differences in clinical symptoms over time) therefore it is expected to be lower than interrater reliability.

Andreasen (1990) also reported the reliability coefficient of each global symptom on the SAPS using Cronbach's alpha. Cronbach's alpha is acceptable for all 4 global symptoms: hallucinations (0.75), delusions (0.66), positive formal thought disorder (0.74), and bizarre behavior (0.79). Cronbach's alpha was also determined for the composite score (the sum of all items) as 0.48. Andreasen and colleagues (1990)

conclude that this score suggests that positive symptoms are less highly correlated than negative symptoms.

The Brief Psychiatric Rating Scale

The Brief Psychiatric Rating Scale was developed to provide a quick and efficient and assessment tool for the evaluation of symptom change in psychiatric patients (Overall & Gorham, 1962). It has been widely used in psychiatric research not only because it is a rapid assessment tool, but also because it provides a comprehensive description of the major psychiatric symptoms. It has been recommended for use where efficiency, speed, and economy are important considerations. It has been determined that raters who are familiar with the rating scale can make the required judgments and complete the instrument in less than five minutes following a clinical interview.

The Brief Psychiatric Rating Scale has gone through several revisions during the course of its development (Gorham & Overall, 1960, 1961). The current scale consists of 16 symptom constructs that resulted from factor analyses of two larger sets of items, namely Lorr's Multidimensional Scale for Rating Psychiatric Patients (MSRPP) (Lorr, Jenkins, & Holsopple, 1953) and Inpatient Multidimensional Psychiatric Scale (IMPS) (Lorr, McNair, Klett, & Lasky, 1960). Examples of the 16 items include somatic concern, anxiety, emotional withdrawal, suspiciousness, hallucinatory behavior, and uncooperativeness. According to the authors, it is important that raters become familiar with the definitions and delineations of each symptom area as outlined by them. Ratings of some items (i.e., tension, mannerisms and posturing, motor retardation) can be made on the basis of observation alone. Whereas other items (i.e., guilt feelings, grandiosity,

unusual thought content) must be rated based on more directive interview questions and the verbal report of the patient. Each item is rated on a 7-point Likert scale ranging from (1) not present to (7) extremely severe. Each individual score provides a sense of the "degree of pathology" (p. 807) in each of the 16 symptom areas. The authors suggest using a "total pathology" score, which is the simple sum of ratings on all 16 items.

Overall & Gorham (1962) provide BPRS interrater reliability scores based on ratings by two independent clinicians on 83 "newly admitted schizophrenic patients" (p. 811). Examples of the interrater reliability scores on each of the 16 BPRS items include the following: somatic concern, r = .81; anxiety, r = .86; guilt feelings, r = .87; depressive mood, r = .76; uncooperativeness, r = .68, and unusual thought content, r = .83. No information concerning test-retest reliability or internal consistency has been provided for this instrument.

Data Analysis

An Exploratory Factor Analysis (EFA) of the items in the SANS, SAPS and BPRS was performed to determine the presence of specific symptom "factors." As outlined in the Research Hypotheses section, it was predicted that the same four-symptom factor solution would be found as in the Shtasel et al. (1992b) study.

A Cluster Analysis of specific patients and their four symptom factors scores was performed to determine the presence of specific subtypes or "clusters" of patients. As outlined in the Research Hypotheses section, it was predicted that three clusters of patients would be produced as in the Shtasel et al. (1992b) study.

A Chi-Square Analysis was performed to determine if there was an association between cluster group and premorbid adjustment group, and an interpretation of cell frequencies was carried out to determine which cells were associated.

Lastly, planned comparisons were performed to test the specific predictions outlined in the Research Hypotheses section concerning differences between the three premorbid groups (deteriorating, stable-good, stable-poor) and clinical symptomatology. Four planned comparisons were done to determine differences in negative symptoms, thought disorder/bizarre behavior, hallucinations/Schneiderian first-ranked symptoms, and paranoia between the groups. Specifically, one planned comparison tested the hypothesis that the deteriorating group would evidence the most severe negative symptoms, compared to the stable-good or stable-poor groups. Two planned comparisons tested the hypothesis that the stable-good group would evidence the most severe thought disorder/bizarre behavior and paranoia compared to the deteriorating or stable-poor groups. One planned comparison tested the hypothesis that the stable-poor group would evidence the most severe hallucinations/Schneiderian first-rank symptoms compared to the deteriorating or stable-good group.

RESULTS

Demographics

A total of 86 subjects ranged in age from 18-48 years (mean = 26.44 years, sd = 7.14). Sixty-six percent of the subjects were male (n = 57) and 34% percent were female (n = 29). The majority of the subjects were African-American (n = 52), with the next largest group being Caucasian (n = 30). The remaining four subjects were Asian-American. Level of educational attainment ranged from 8-22 years (mean = 12.98 years, sd = 2.69). Although subjects were enrolled in the study and defined as first-episode because they were experiencing psychotic symptoms for the first time, had not accepted psychiatric treatment in the past, and were neuroleptic naïve, more extensive chart review revealed that some subjects did not meet all three of these criteria. Specifically, it was discovered that ten subjects had been taken to psychiatric emergency rooms in the past (i.e., before study entry) and nine of them had been given neuroleptic medication. None of these subjects remained on medication; therefore, all were free of neuroleptics at time of study participation. It was for this reason, as well is issues of sample size, that a decision was made to include these subjects in the current study. Therefore, at study entry 90% of subjects were neuroleptic naïve (n = 77) and 10% of subjects had been exposed to short duration neuroleptics in the past (n = 9). The average age psychotic symptoms first appeared ranged from 15-48 years (mean = 24.7, sd = 6.87). At study entry, 55% of subjects had a diagnosis of schizophrenia (n = 47), 44% had a diagnosis of schizophreniform disorder (i.e., evidence of psychotic symptoms for less than six months) (n = 38), and 1 % had a diagnosis of schizoaffective disorder (n = 1). Group

means and standard deviations for demographic information are summarized in Table 3. Group frequencies and percentages for demographic information are summarized in Table 4.

Table 3

Means and Standard Deviations of Demographic Information

Variable	Minimum	Maximum	Mean	Standard Deviation
Age	18	48	26.44	7.14
Age of Onset	15	48	24.70	6.87
Education	8	22	12.98	2.69
Father's Education	5	21	13.19	3.39
Mother's Education	7	21	12.81	2.80

Table 4

Frequencies and Percentages of Demographic Information

Variable		Frequency	Percentage
Sex			
	Male	57	66 %
	Female	29	34 %
Race			
	African-American	52	60 %
	Caucasian	30	35 %
	Asian-American	4	5 %
Medication Status			
	Neuroleptic Naïve	77	90 %
	Not Neuroleptic Naïve	9	10 %
Intake Diagnosis			
	Schizophrenia	47	55 %
	Schizophreniform Disorder	38	44 %
	Schizoaffective Disorder	1	1 %

Exploratory Factor Analysis

The SANS, SAPS, and BPRS items were subjected to a principal components Exploratory Factor Analysis (EFA) followed by an orthogonal (i.e., varimax) rotation of the factor pattern. The rotation converged in six iterations. Examination of the scree plot suggested a four-factor solution. Specifically, there was a clear separation between the eigenvalues of the first four factors (13.8, 7.2, 5.7, and 3.6 respectively) and those of the remainder. The most salient loadings of the SANS, SAPS, and BPRS items on the four symptom factors are shown in Table 5. These four factors accounted for 21.3, 11.1, 8.7, and 5.5 percent of the variance in the symptom ratings, respectively. As shown in Table 5, the four factors are easily interpretable.

The first factor (the negative factor) represents the negative symptoms of schizophrenia, otherwise known as the deficit syndrome. Significant loadings on this factor include all but two of the SANS items, the SAPS repetitive or stereotyped behavior item, and the BPRS blunted affect, emotional withdrawal, motor retardation, and mannerisms and posturing items. The second factor (the disinhibition factor) represents symptoms including positive formal thought disorder and bizarre behavior. Significant loadings on this factor include the SAPS thought disorder and bizarre behavior items, the SANS inappropriate affect and grooming and hygiene items, and the BPRS conceptual disorganization, excitement, hostility and uncooperativeness items. The third factor (the positive factor) represents the positive symptoms of schizophrenia, otherwise known as the non-deficit syndrome. Significant loadings on this factor include the hallucinations, delusions, and Schneiderian FRS items on the SAPS, the hallucinatory behavior item on

the BRPS, and no SANS items. The fourth factor (the paranoid factor) represents the paranoid symptoms of schizophrenia. Significant loadings on this factor include the SAPS persecutory delusions, global rating of delusions, delusions of guilt and sin and aggressive and agitated behavior items, the BPRS anxiety, guilt, depression, suspiciousness and tension items, and no items on the SANS. As predicted, all four factors were consistent with the original Exploratory Factor Analysis done by Shtasel et al. (1992) with the exception of factor four. Specifically, Shtasel et al. (1992) described factor four as a paranoia/grandiosity factor. In the present study, the grandiosity items did not load significantly on factor four, but instead evidenced weak loadings on factor two.

The reliability coefficient for each factor was calculated using Cronbach's alpha. Cronbach's alpha was high for all 4 factors: factor 1 – negative (0.95); factor 2 – disinhibition (.87); factor 3 – positive (.86); factor 4 – paranoid (.75).

Table 5

SANS, SAPS, BPRS Factor Analysis

Scales	Salient Factor Loading
Factor 1 – The Negative Factor (Negative Symptoms)	
SANS	
Global Rating of Affective Flattening	.82
Lack of Vocal Inflections	.81
Poverty of Speech	.78
Global Rating of Alogia	.78
Paucity of Expressive Gestures	.78
Unchanging Facial Expression	.76
Decreased Spontaneous Movements	.76
Increased Latency of Response	.73
Social Inattentiveness	.72
Affective Nonresponsivity	.67
Poor Eye Contact	.66
Global Rating of Attention	.65
Physical Anergia	.65
Poverty of Content of Speech	.64
Blocking	.60
Recreational Interests	.56
Relationships with Friends	.56
Global Rating of Anhedonia/Asociality	.55
Global Rating of Avolition/Apathy	.53
Ability to Feel Intimacy	.52
Inattentiveness during Mini-Mental Status Exam	.45
Impersistence at Work/School	.42
Sexual Activity	.34
SAPS	
Repetitive or Stereotyped Behavior	.40
BPRS	
Blunted Affect	.89
Emotional Withdrawal	.75
Motor Retardation	.58
Mannerisms and Posturing	.37
Disorientation	.28

Table 5 (cont'd)

Factor 2 – The Disinhibition Factor (Thought Disorder/Bizarre Behavior)	
SANS	
Inappropriate Affect	.62
Grooming and Hygiene	.42
SAPS	
Global Rating of Thought Disorder	.84
Derailment	.72
Illogicality	.72
Tangentiality	.71
Incoherence	.61
Circumstantiality	.55
Pressure of Speech	.49
Clanging	.43
Distractible Speech	.42
Global Rating of Bizarre Behavior	.42
Somatic Delusions	.32
Somatic or Tactile Hallucinations	.30
Clothing and Appearance	.30
Grandiose Delusions	.29
Social and Sexual Behavior	.27
BPRS	
Conceptual Disorganization	.77
Excitement	.62
Hostility	.46
Uncooperativeness	.41
Grandiosity	.34
Factor 3 – The Positive Factor (Hallucinations/Schneiderian FRS)	
SANS	
No items	
SAPS	
Auditory Hallucinations	.81
Global Rating of Hallucinations	.81
Thought Insertion	.70
Delusions of Mind Reading	.68
Thought Broadcasting	.62
Voices Conversing	.59

Table 5 (cont'd)

Voices Commenting	.56
Thought Withdrawal	.54
Delusions of Being Controlled	.49
Delusions of Reference	.37
Visual Hallucinations	.36
Olfactory Hallucinations	.32
BPRS	
Hallucinatory Behavior	.82
Unusual Thought Content	.32
Factor 4 – The Paranoid Factor	
SANS	
No items	
SAPS	
Persecutory Delusions	.58
Global Rating of Delusions	.56
Delusions of Guilt or Sin	.55
Aggressive and Agitated Behavior	.53
BPRS	
Anxiety	.79
Guilt Feelings	.58
Depressed Mood	.46
Suspiciousness	.43
Tension	.41
Somatic Concern	.35

Cluster Analysis of Patients

The Exploratory Factor Analysis (EFA) generated a regression factor score (with a mean of zero) for every subject on each of the four symptom factors. The four factor scores for each subject were then subjected to a K-means Cluster Analysis to determine whether they could differentiate subgroups of patients. The factor scores were used as the basis for clustering subjects (i.e., as opposed to the original symptom items) to ensure that the clusters of patients differed on symptoms that represent independent dimensions of the illness. This method is consistent with Shtasel et al. (1992). The Cluster Analysis of the four symptom factor scores (i.e., negative, disinhibition, positive, paranoid) produced three clusters of patients. The solution required five iterations. Values of the cluster centers (i.e., mean regression factor score) for each of the four symptom factors are shown in Table 6.

As shown in Figure 1, each cluster evidenced a different factor profile. Specifically, cluster one represents a group of patients with predominantly negative symptoms. Cluster two represents a group of patients with predominantly disinhibition symptoms (i.e., thought disorder and bizarre behavior) and paranoid symptoms. Cluster three represents a group of patients with predominantly positive symptoms (i.e., hallucinations and Schneiderian FRS). As predicted, all three clusters were consistent with the original Cluster Analysis done by Shtasel et al (1992).

As shown in Figure 2, 29 subjects (34%) were in cluster one (negative), 18 subjects (21%) were in cluster two (disinhibition/paranoia), and 39 (45%) were in cluster three (positive).

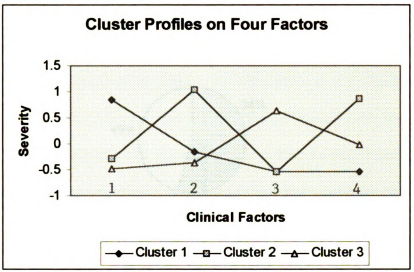
Table 6

Cluster Centers of Four Symptom Factors

	Cluster 1	Cluster 2	Cluster 3
Factor 1 (negative)	.84	-.29	-.49
Factor 2 (disinhibition)	-.16	1.04	-.36
Factor 3 (positive)	-.53	-.54	.64
Factor 4 (paranoid)	-.53	.87	-.01

Figure 1

Cluster Profiles on Four Factors

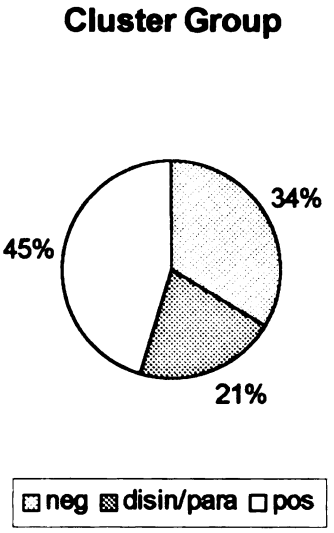


Factor 1 - negative symptoms
Factor 2 - disinhibition symptoms (thought disorder/bizarre behavior)
Factor 3 - positive symptoms (hallucinations and Schneiderian FRS)
Factor 4 - paranoid symptoms

Cluster 1 - prominent negative symptoms
Cluster 2 - prominent disinhibition and paranoid symptoms
Cluster 3 - prominent positive symptoms

Figure 2

Cluster Group Membership



Cluster 1: 34% prominent negative symptoms (n = 29)

Cluster 2: 21% prominent disinhibition/paranoid symptoms (n = 18)

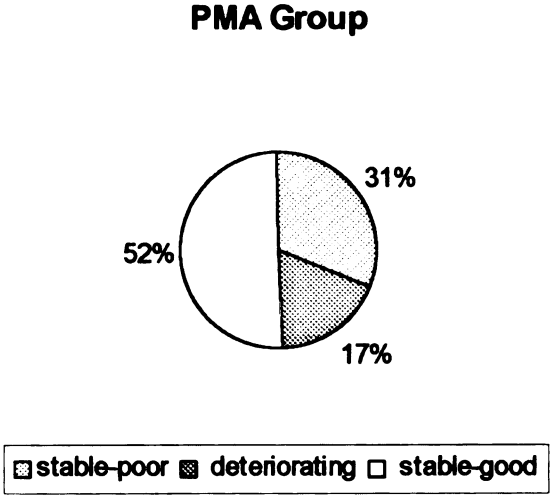
Cluster 3: 45% prominent positive symptoms (n = 39)

Patterns of Premorbid Adjustment (PMA)

As outlined in the Methods section, subjects were classified into three patterns of premorbid adjustment: deteriorating, stable-good, and stable-poor. Subjects were classified as deteriorating if they had a pattern of worsening scores over the premorbid periods that totaled a two-point change. All other subjects were classified as stable, and the mean PMA score (2.0) was used as a cutoff point to divide subjects into the stable-good or stable-poor group. As shown in Figure 3, 15 subjects (17%) had a deteriorating pattern of premorbid adjustment, 44 subjects (52%) had a stable-good pattern, and 27 subjects (31%) had a stable-poor pattern. Demographic information for the PMA groups is presented in Table 7.

Figure 3

Premorbid Adjustment Group Membership



Stable-poor: 31% (n = 27)

Deteriorating: 17% (n = 15)

Stable-good: 52% (n = 44)

Table 7

Demographic Information for PMA Groups

	Stable-Poor	Deteriorating	Stable-Good
Sex (frequency/percentage)			
Male	18 (67 %)	14 (93 %)	25 (57 %)
Female	9 (33 %)	1 (7 %)	19 (43 %)
Race (frequency/percentage)			
African-American	18 (67 %)	8 (53 %)	26 (59 %)
Caucasian	7 (26 %)	6 (40 %)	17 (39 %)
Asian-American	2 (7 %)	1 (7 %)	1 (2 %)
Education (mean/sd)	13.11 (3.08)	11.87 (2.07)	13.27 (2.57)

Chi-Square Test

A Pearson's Chi-Square Test of Independence was performed to determine if there was an association between cluster group (i.e., cluster 1-negative, cluster 2-disinhibition/paranoia, cluster 3-positive) and premorbid adjustment group (i.e., deteriorating, stable-good, stable-poor). The number of subjects in each cluster group differed as a function of PMA group. The overall difference in proportions was significant, chi-square (4, 86) = 31.9, $p \leq .0001$. A contingency table that outlines cell frequencies and percentages is provided in Table 8. Further interpretation of cell frequencies suggested a significant relationship between the deteriorating group and cluster 1-negative (expected count 5, count 13), the stable-good group and cluster 2-disinhibition/paranoia (expected count 9, count 16), and the stable-poor group and cluster 3-positive (expected count 12, count 18).

Table 8

Chi-Square Contingency Table of Cell Frequencies and Percentages

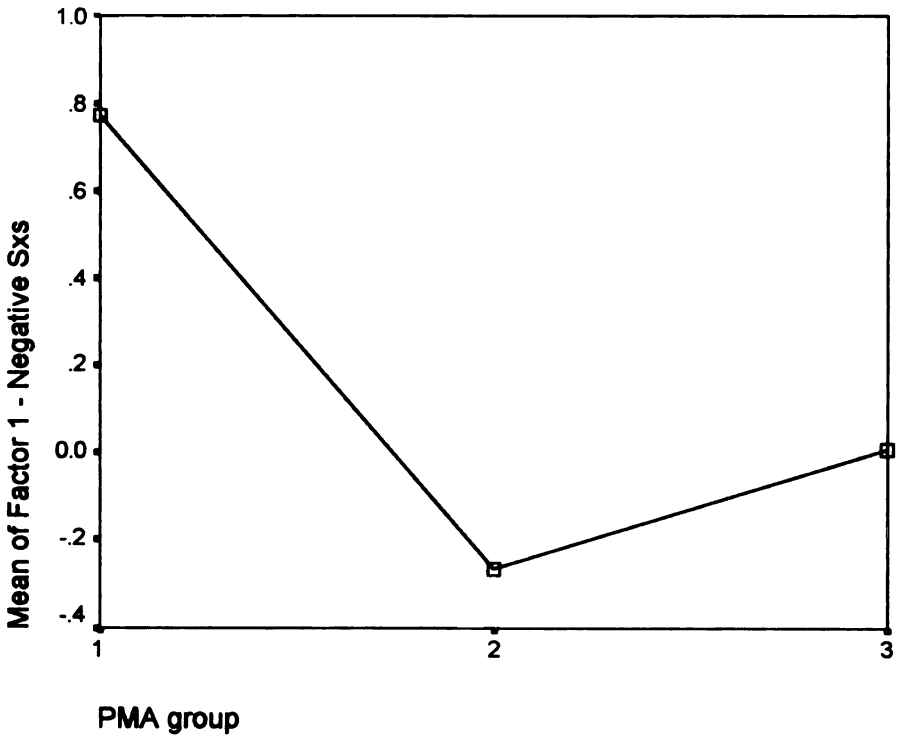
		PMA Group		
		Deteriorating	Stable-Good	Stable-Poor
Cluster Group				
Negative	Count	13	9	7
	Expected Count	5	15	9
	Percentage	45 %	31 %	24 %
Disinhibition/ Paranoia	Count	0	16	2
	Expected Count	3	9	6
	Percentage	0 %	89 %	11 %
Positive	Count	2	19	18
	Expected Count	7	20	12
	Percentage	5 %	49 %	46 %

Planned Comparisons

Lastly, four planned comparisons were performed to test the specific predictions outlined in the Research Hypotheses section concerning differences between the three premorbid groups (i.e., deteriorating, stable-good, stable-poor) and clinical symptomatology. Specifically, one planned comparison confirmed the hypothesis that the deteriorating group had the most severe negative symptoms, compared to the stable-good or stable-poor groups ($t = -3.4$, $p \leq .001$) (std. error = .535), ($d = -.97$) (see Figure 4). Two planned comparisons suggested that the stable-good group had the most severe disinhibition symptoms and paranoid symptoms, compared to the deteriorating or stable-poor groups, although these differences were not statistically significant ($t = -1.5$, $p \leq .136$) (std. error = .438), ($d = -.32$); ($t = -1.7$, $p \leq .084$) (std. error = .437), ($d = -.37$) respectively (see Figure 5 and Figure 6). And, one planned comparison confirmed the hypothesis that the stable-poor group had the most severe hallucinations/Schneiderian first-ranked delusions compared to the deteriorating or stable-good groups ($t = -2.89$, $p \leq .005$) (std. error = .469), ($d = -.67$) (see Figure 7).

Figure 4

Means of Factor 1 by PMA group



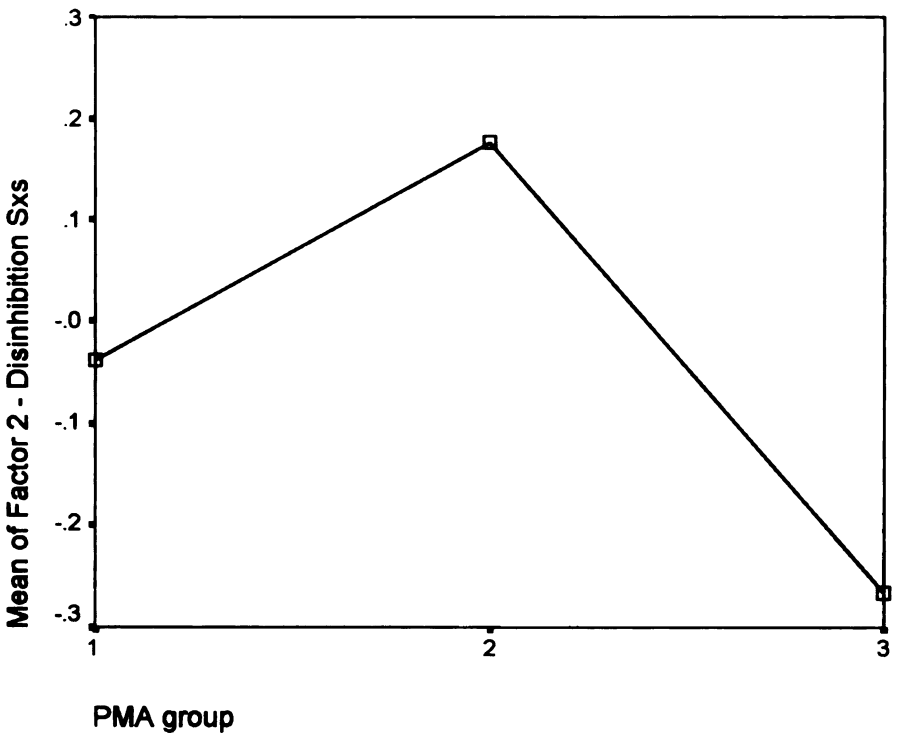
PMA group 1 = deteriorating

PMA group 2 = stable-good

PMA group 3 = stable-poor

Figure 5

Means of Factor 2 by PMA Group



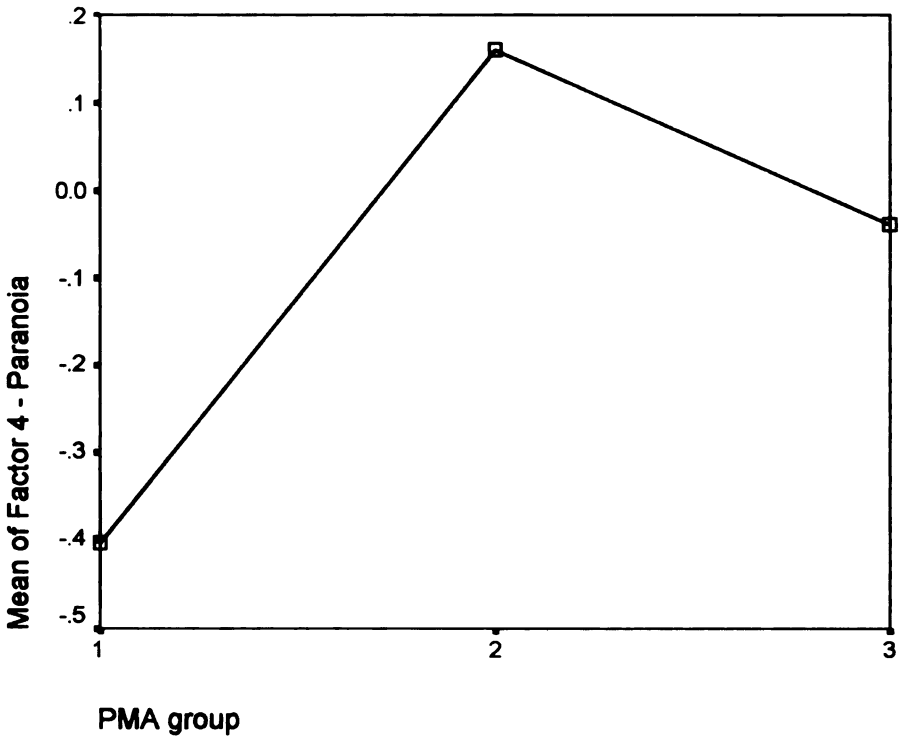
PMA group 1 = deteriorating

PMA group 2 = stable-good

PMA group 3 = stable-poor

Figure 6

Means of Factor 4 by PMA Group



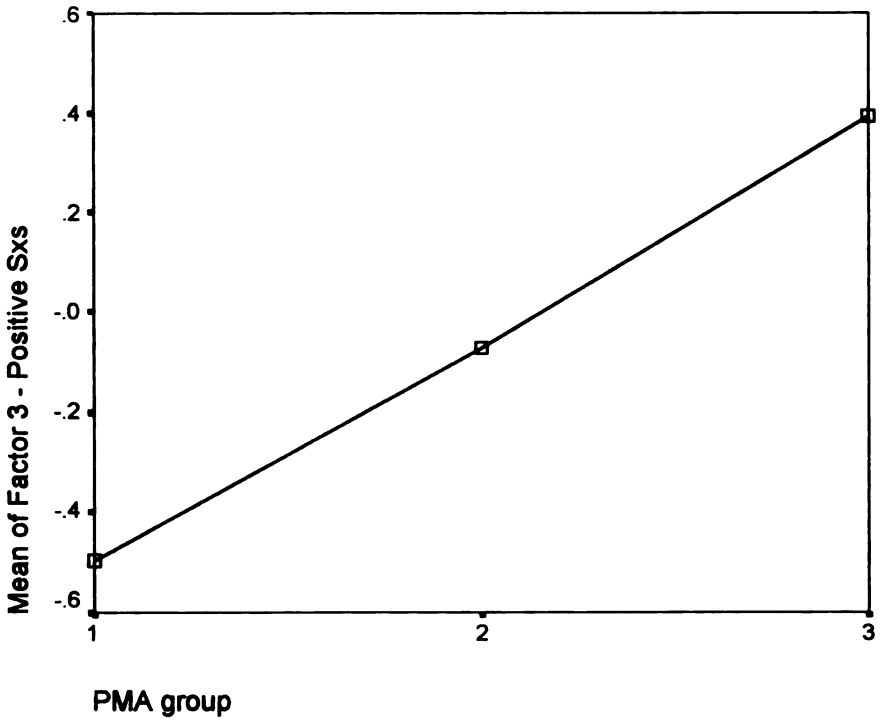
PMA group 1 = deteriorating

PMA group 2 = stable-good

PMA group 3 = stable-poor

Figure 7

Means of Factor 3 by PMA Group



PMA group 1 = deteriorating

PMA group 2 = stable-good

PMA group 3 = stable-poor

DISCUSSION

The goals of the present study were twofold. First, it attempted to strengthen the existing literature on clinical phenomenology of schizophrenia by providing additional evidence for the presence of phenomenological subtypes. Second, it attempted to further our knowledge of the clinical course of schizophrenia by integrating data from the period before illness onset (i.e., premorbid adjustment) and the period during illness onset (i.e., first-episode psychosis). Specifically, it examined the relationships between three patterns of premorbid adjustment (i.e., deteriorating, stable-good, stable-poor) and the presence of specific schizophrenic symptomatology (i.e., negative symptoms, hallucinations, Schneiderian FRS, thought disorder, bizarre behavior, and paranoia) during first-episode psychosis in an attempt to delineate specific etiologies or developmental pathways of schizophrenia. The results of the present study achieved both of the aforementioned goals. Despite these encouraging findings, issues of postulating specific etiologies or developmental pathways of schizophrenia is a complex endeavor and therefore warrants careful consideration and discussion.

With respect to the clinical phenomenology of schizophrenia, this study provides additional support for the presence of phenomenological subtypes. With the growing sophistication of both symptom rating scales and statistical procedures over the years, researchers have been able to abandon the simple positive/negative (Andreasen & Olson, 1982; Hughlings-Jackson, 1931) Type I/Type II (Crow, 1980, 1985), and deficit/non-deficit (Carpenter et al., 1988) dichotomies and investigate more complex patterns of symptom presentation. The discovery of several symptom factors (Liddle, 1987, Bilder

et al. 1985, Gur et al 1991) has guided researchers away from the notion that positive and negative symptoms of schizophrenia are in someway bipolar, like depression and mania (Shtasel et al, 1992). Instead positive and negative symptoms of schizophrenia are now thought to be distinct processes, which may occur simultaneously in some individuals. This realization has fueled the development of more complex symptom characterization in schizophrenia. To that end, the factor analysis carried out in the present study confirmed the presence of four symptom factors. As predicted, these factors were similar to those found by Shtasel et al (1992) and included: a negative factor, a "disinhibition" factor (thought disorder, bizarre behavior), a positive factor (hallucinations/Schneiderian FRS) and a paranoid factor.

The only difference between the factor analysis results in the present study and those in the Shtasel et al. (1992) study is that Shtasel and her colleagues' fourth factor included significant loadings on both paranoia and grandiosity items; however, in the current analysis the two grandiosity items had insignificant loadings on factor two. Further investigation of this suggests that differences in the sample may responsible. That is, 65% of the subjects in the Shtasel et al. (1992) study were not first-episode, instead having had schizophrenia for an average of approximately 10 years. It is possible that individuals who have had schizophrenia longer may be more likely to develop grandiose delusions as a defense against the feelings of powerlessness and inadequacy that may arise as a result of living with schizophrenia long-term. In other words, development of an exaggerated self-opinion or conviction of special powers or abilities may develop secondarily, to help the individual with schizophrenia cope with and find some meaning (albeit delusional) in their psychotic symptoms. In addition, when

symptoms of paranoia and grandiosity are present, it makes sense that they would load on the same factor, as they both constitute a narcissistic world-view.

The cluster analysis carried out in the present study confirmed the presence of three groups of patients. As predicted, these clusters were similar to those found by Shtasel et. al (1992) and included: a cluster one group with predominantly negative symptoms; a cluster two group with predominantly disinhibition symptoms (thought disorder and bizarre behavior) and paranoid symptoms; and a cluster three group with predominantly positive symptoms (hallucinations and Schneiderian FRS). Several issues warrant discussion.

First, despite the inclusion of only first-episode, 90% neuroleptic naive patients, there was a group with predominantly negative symptoms. This provides evidence for the fact that negative symptoms can manifest early in the illness and are therefore not always a result of medication effects, institutionalization, stigma, or chronicity.

Second, prominent disinhibition and paranoid symptoms were both displayed in cluster two. It may be that symptoms of disinhibition or disorganization such as thought disorder and bizarre behavior exacerbate paranoia. That is, both the inability to communicate one's thoughts clearly and the presence of bizarre behaviors are overt, easily noticeable symptoms and there presence may cause the person with schizophrenia to have trouble interacting with others in the world. Stated more specifically, when individuals with schizophrenia attempt to communicate in a bizarre or unclear way, they may receive negative reactions from others that fuel feelings of paranoia.

Next, with respect to comparing the individuals in each cluster in the two studies there exist several differences. Most notable is the fact that in the Shtasel et al. (1992)

study, the largest number of patients were in cluster one (45%), whereas in the present study the largest number of patients were in cluster three (45%). It may be that the Shtasel et al (1992) study evidenced more cluster one patients than the present study (45% versus 34%) because, as mentioned earlier, the majority of its' subjects were individuals with chronic schizophrenia. And, as can be the case in chronic patients, negative symptoms may develop as a result of long-term use of neuroleptic medication, effects of chronicity of illness, stigma, institutionalization, and a general withdrawal and sense of hopelessness over time. Furthermore, it may be that most patients were in cluster three in the present study because of their first-episode status. That is, individuals who are experiencing the positive symptoms of schizophrenia such as auditory, tactile, olfactory or visual hallucinations and delusions of reference, mind reading, or thought broadcasting may be more likely to be referred for inpatient treatment by family members, the legal system, or other health professionals. In contrast, individuals with a more benign form of the illness may be able to remain unnoticed by family members or be maintained on an outpatient basis and therefore would be less likely to be represented in the present study.

Lastly, the aforementioned factor analysis of symptoms provides statistical support for the existence of clinical subtypes in schizophrenia. However, for the clinician, the results of a cluster analysis provides even more compelling evidence for the existence of clinical subtypes given the fact that it yields distinct subgroups of individuals. Overall, these results support the notion that schizophrenia can manifest itself in a number of ways. There is no doubt that the patient in cluster one would look very different than the patient in clusters two or three. The remaining statistical

procedures in this study were designed to understand the role of premorbid adjustment in helping to explain why two people with a diagnosis of schizophrenia can look so very different.

Subjects were classified into three patterns of premorbid adjustment based on their levels of functioning in several areas (e.g., scholastic performance and adaptation, peer and social-sexual relationships) across childhood (0-11 years), early adolescence (12-15 years), late adolescence (16-18 years) and adulthood (19 years and beyond). The present study found that 17 % of the subjects had a deteriorating pattern of premorbid adjustment. That is, they evidenced a slow, insidious decline in functioning over time. Fifty-two percent of subjects had a stable-good pattern of premorbid adjustment identified by consistently adequate-good levels of functioning from childhood until onset of first psychotic symptoms. Finally, 31% of subjects had a stable-poor pattern of premorbid adjustment identified by consistently low levels of functioning from childhood until onset of first psychotic symptoms.

There were significantly more males than females in both the deteriorating (14 males, 1 female) and stable-poor (18 males, 9 females) groups in comparison to the stable-good group. These findings are consistent with numerous studies that suggest that males evidence poorer premorbid adjustment than females (Klorman et al., 1977; Lewine, 1981; Loranger, 1984; Shtasel et al., 1992a; Larsen 1996). Possible explanations for this include males' greater incidence of brain insult and morphology in childhood (Nasrallah & Wilcox, 1989, Lewine et al., 1990) and differences in social factors such as depth of affect (Loranger, 1984; Shtasel et al., 1992). Gender stereotyping may make it more difficult for boys to discuss their difficulties and the feelings surrounding them than girls,

which may have a cumulative effect and result in even greater problems with functioning.

In addition, there were significantly more African-American individuals than those of other races in the stable-poor group compared to the other premorbid adjustment groups. It is suggested that these racial differences may be a result of socio-economic issues including greater poverty, less access to resources such as adequate health care and childcare, poor schooling, and issues of racial prejudice experienced by the African-American community in West Philadelphia.

Another notable difference between the premorbid adjustment groups included average level of educational attainment. The deteriorating group evidenced a lower average of educational attainment than the other two premorbid groups (deteriorating = 11.9 years, stable-good = 13.3 years, stable-poor = 13.1 years). This suggests that individuals in the deteriorating group were less likely to have finished high school than those in the other two groups. This inability to finish high school may be a result of the deteriorating groups' difficulty adjusting to their insidious decline in functioning. In contrast, the stable-poor group, who are accustomed to experiencing difficulties, may be better able to complete high school (even though their level of achievement is low) as a result of longer-term adjustment to poor levels of functioning.

A chi-square test was then performed to determine if there was an association between premorbid adjustment group and cluster group. In other words, if an individual was in a particular premorbid group were they likely to also be in a particular cluster group. As predicted, the results of the present study suggested several significant relationships.

First, there was an association between the deteriorating group and cluster one (negative). This suggests that individuals who experienced a slow, insidious decline in functioning over time are also likely to evidence prominent negative symptoms during first-episode psychosis. A planned comparison provided further evidence for this finding by confirming the hypothesis that the deteriorating group had the most severe negative symptoms, compared to the stable-good or stable-poor groups. These results are consistent with findings by both Haas and Sweeney (1992) and Larsen et al. (1996b, 1998) that those with an insidious decline in functioning had a trend for more severe anhedonia and social withdrawal than those in other premorbid groups. The relationship between poor premorbid adjustment and negative symptomatology has been repeatedly demonstrated in both chronic (Andreasen & Olsen, 1982; Andreasen et al., 1990; Dworkin et al., 1987; Kay & Lindenmayer, 1987; McGlashan & Fenton, 1992; Pogue-Geile & Harrow, 1984) and first-episode schizophrenia (Dalkin et al., 1994; Larsen et al., 1996a; Peralta et al., 1991, 1992). Given this body of knowledge one might expect to find a relationship between cluster one (negative) and the stable-poor group instead of the deteriorating group. Instead there was an association between the stable-poor group and cluster three (positive). A planned comparison confirmed the hypothesis that the stable-poor group had the most severe hallucinations and Schneiderian FRS compared to the deteriorating or stable-good groups.

The results of the present study suggest that the relationship between premorbid adjustment and clinical symptomatology is more complex than was originally proposed in research designs that employed a simple good versus bad premorbid adjustment dichotomy. In more sophisticated designs, where poor-premorbid adjustment has been

further broken down into deteriorating versus stable-poor one finds differences between the two groups. The major difference is that those in the deteriorating group were functioning adequately in childhood or early adolescence, with a decline in functioning not occurring until late adolescence or adulthood. In contrast, the stable-poor group did not have a period of adequate functioning in early life, and instead were always functioning poorly. From a developmental perspective, a period of adequate functioning in childhood may provide a protective mechanism against the development of severe psychotic symptoms such as hallucinations and Schneiderian FRS. That is, individuals who have always been withdrawn and struggling with issues of competence and adaptation in school and with peers may be more likely to escape into psychosis and create delusional realities. In comparison, children who did not develop a decline in functioning until later in life may be better able to remain in touch with reality and therefore negative symptoms such as blunted affect and social withdrawal are more likely than symptoms of overt psychosis. Also, if one conceptualizes the symptoms of schizophrenia along a severity continuum, with negative symptoms as less severe (with respect to a break from reality) than positive symptoms, then it makes sense that those who have been sicker longer (stable-poor) would be more likely to develop severe positive symptoms. Larsen and colleagues (1998) provide support for this notion in their report that individuals with a long duration of untreated symptoms appear to be more likely to develop bizarre hallucinations and delusions than those with a short duration of untreated symptoms. Overall, this suggests that the stable versus unstable dichotomy is more predictive than the simple good versus bad.

There was also an association between the stable-good group and cluster two (disinhibition/paranoia). Two-planned comparisons suggested a trend that the stable-good group had the most severe disinhibition symptoms and paranoid symptoms, compared to the deteriorating or stable-poor groups, although these results were not statistically significant. Traditional analyses of significance, such as those used in the present study, may have contributed to the probability of making a type II error (i.e., the hypotheses were in fact true, despite insignificant results). In any event, these trends are consistent with previous studies that suggest individuals with paranoid schizophrenia have better premorbid adjustment than those with other subtypes of schizophrenia (Deister & Marneros, 1993; Magaro, 1981; Zigler, Levine, & Zigler, 1977). Additional studies have reported that individuals with paranoid schizophrenia are more likely to have had higher levels of social competence and a stable socio-sexual partner before onset of illness than non-paranoids (Deister & Marneros, 1993, Zigler & Levine, 1983). This relationship between good premorbid adjustment and disorganized and paranoid symptoms may exist because of their interpersonal nature. That is, individuals with good premorbid adjustment were involved in social relationships and active in social institutions such as school or work. They likely had more opportunity to interact with others than those in the deteriorating or stable-poor groups and as a result, manifest the more interpersonal symptoms of schizophrenia such as thought disorder (i.e., difficulty communicating with others) and paranoia (i.e., fear that other people are out to harm them).

Overall, these findings provide support for the existence of three developmental pathways of schizophrenia. It appears that patterns in early development are associated

with the types of psychotic symptoms one manifests in first-episode psychosis. More specifically, the results of the present study provide evidence for a "continuum of severity" model of schizophrenia. That is, at first-episode the sickest premorbid group (stable-poor) evidenced the most severe symptoms (positive); the moderate premorbid group (deteriorating) evidenced moderate symptoms (negative); and the healthiest premorbid group (stable-good) evidenced the mildest symptoms (thought disorder/paranoia).

This information can help to guide us in early detection, prevention, and treatment of first-episode schizophrenia. Clinicians have begun to target the period before the onset of frank psychotic symptoms as an important time for intervention. Early intervention in psychosis has been deemed important from several perspectives. First, from a biological perspective, the brain is seen as retaining some measure of plasticity early in the illness, therefore early intervention may help to prevent both structural and functional deterioration (McGlashan, 1998). Second, with respect to treatment, a number of researchers have found that the earlier intervention takes place, the more successful the outcome (Edwards et al., 1998; Inoue et al., 1986; Loebel et al., 1992; McGlashan, 1996; McGlashan & Johannessen, 1996; McGorry et al., 1996; Wyatt, 1991). Similarly, numerous studies have found significant inverse correlations between the duration of untreated psychosis and better outcome (Crow et al. 1986; Lo & Lo, 1977; Moscareli, 1994; Rabiner et al., 1986). And from a purely humane perspective, as articulated by McGlashan and Johannessen (1996) " Bringing treatment more rapidly to a person who has been psychotic is in itself enough to justify early detection efforts" (p. 201). In general, Birchwood, Todd and Jackson (1998) define the early phase of psychosis

(including the period of untreated psychosis) as the 'critical period' because it is at this time that psychological, psychosocial, and biological influences are developing and are at their maximum plasticity.

In one of the first programs of its kind, Falloon and colleagues in England (Falloon, 1992; Falloon et al., 1996) used prodromal symptom indicators to identify individuals at risk for psychosis. Early intervention with this population resulted in a reduction of florid schizophrenia. McGorry and colleagues have recently developed the Early Psychosis Prevention and Intervention Center (EPPIC) in Australia, which is pioneering the treatment of individuals in the prodromal stage of schizophrenia (McGorry et al., 1996; Yung & McGorry, 1996; Yung et al., 1996). EPPIC has successfully decreased the duration of untreated psychosis and improved one-year outcome measures in their study participants in comparison to a similar group of individuals with first-episode psychosis who received treatment before the early detection program was instituted. As stated by McGorry et al. (1998) "Psychotic symptoms occur on a continuum with normal states of mind" (p. 15). This points to the development of a new ideology in the treatment of psychosis, which suggests that sub-threshold symptoms can be detected, and have some predictive value for the subsequent development of psychosis (Allen et al. 1987; Chapman & Chapman, 1980).

Despite the encouraging findings in the present study, several methodological issues warrant discussion. First, an increase in sample size would provide more robust statistical evidence. Second, because of the retrospective nature of gathering premorbid adjustment data, issues regarding accuracy of recall are raised. As discussed by Fava and Kellner (1991), a long-delay between the first noticeable changes in behavior and the

onset of psychotic symptoms can negatively affect recall. Several researchers describe the influence of "effort after meaning" which refers to the tendency of patients and families to identify one event that marked the change in behavior and dating their histories from that event (Hirsch et al 1992; Tennant, 1985). Yung and McGorry (1996) report other factors that may influence what is reported including family guilt at not noticing changes sooner, and denial of difficulties in an attempt to cope with the onset of psychosis.

Schizophrenia is one of society's most severe and costly medical conditions (McGlashan, 1996). Further research is needed to identify those at risk for developing psychotic disorders and provide treatment in the early phases of the illness. Both large-scale meta-analytic studies and long-term, high-risk models can help to further identify causal links between early development and first-episode psychotic symptoms. Finally, attention to the integration of data from various developmental periods can help us better understand that psychotic symptoms may not be random biological mechanisms, but instead may have meaning in the context of a developmental history. Continued attempts must be made to formulate an integrated conceptualization of the developmental processes underlying psychotic symptomatology.

APPENDICES

APPENDIX A

Table 1

Prodromal Features in First Episode Psychosis (Yung & McGorry, 1996)

1.	Reduced concentration, attention
2.	Reduced drive and motivation, anergia
3.	Depressed mood
4.	Sleep disturbance
5.	Anxiety
6.	Social withdrawal
7.	Suspiciousness
8.	Deterioration in role functioning
9.	Irritability

APPENDIX B

Table 2

Psychosocial Indicators of Vulnerability to Schizophrenia (Hartmann et al., 1984)

1. UNUSUAL ANXIETY: inconsolable baby; world perceived as scary; frequent nightmares; continuing anxiety in school

2. NEOPHOBIA: fear of new things; reacting to familiar as if new; failure to enter familiar situations with decreased apprehension

3. LACK OF HISTORICITY: lack of sense of self continuing over time; poor goal-directed behavior; lack of ambition

4. INAPPROPRIATE AGGRESSION: random aggression; cruelty; unusually aggressive fantasies

5. INAPPROPRIATE ANGER: self-directed anger; denial of anger when appears angry to others; inexplicable bursts of anger

6. FLAT AFFECT: affective disturbance in direction of flat of inappropriate affect

7. ANHEDONIA: inability to enjoy anything; lack of hobbies; lack of pleasure in play

8. LACK OF OBJECT CONSTANCY: lack of ability to relate; difficulty in shifting away from family to friends; overclinging or defensive overindependence

9. DIFFICULTY IN INTERPERSONAL RELATIONSHIPS: parents find it hard to "reach" child; considered undependable; no or little peer group relations

10. PERMEABLE BOUNDARIES: easily distracted; excessive daydreaming; tendency to tangential thinking; poorly integrated body image

11. LACK OF COMPETENCY: delays in developmental milestones; poor schoolwork; poor sense of competence

12. CHEMICAL OR NEUROLOGIC ABNORMALITIES: disturbed sleep; disturbed gait; neurologic soft signs; unusual reactions to drugs or alcohol

APPENDIX C:

THE PREMORBID ADJUSTMENT SCALE

(Cannon-Spoor, Potkins, & Wyatt, 1982)

THE PREMORBID ADJUSTMENT SCALE (PMA)

CHILDHOOD (UP THROUGH AGE 11)

1. Sociability and Withdrawal
   - 0 Not withdrawn, actively and frequently seeks out social contacts.
   - 1
   - 2 Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize.
   - 3
   - 4 Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others but does not seek it.
   - 5
   - 6 Unrelated to others, withdrawn and isolated, avoid contact.

2. Peer Relationships
   - 0 Many friends, close relationships with several.
   - 1
   - 2 Close relationships with a few friends (one or two), casual friendships with others.
   - 3
   - 4 Deviant friendship patterns – friendly with children younger or older only, or relatives only, or casual relationships only.
   - 5
   - 6 Social isolate, no friends, not even superficial relationships.

3. Scholastic Performance
   - 0 Excellent student.
   - 1
   - 2 Good student.
   - 3
   - 4 Fair student.
   - 5
   - 6 Failing all classes.

4. Adaptation to School
   - 0 Good adaptation, enjoys school, no or rare discipline problems, has friends at school, likes most teachers.
   - 1
   - 2 Fair adaptation, occasional discipline problems, not very interested in school but no/or rare truancy, has friends in school but does not often take part in extracurricular activities.
   - 3
   - 4 Poor adaptation, dislikes school, frequent discipline problem.

5

6 Refuses to have anything to do with school – delinquency or vandalism directed against school.

ADOLESCENCE (EARLY, AGES 12-15)

1. Sociability and Withdrawal
   - 0 Not withdrawn, actively and frequently seeks out social contacts.
   - 1
   - 2 Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize.
   - 3
   - 4 Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others but does not seek it.
   - 5
   - 6 Unrelated to others, withdrawn and isolated, avoid contact.

2. Peer Relationships
   - 0 Many friends, close relationships with several.
   - 1
   - 2 Close relationships with a few friends (one or two), casual friendships with others.
   - 3
   - 4 Deviant friendship patterns – friendly with children younger or older only, or relatives only, or casual relationships only.
   - 5
   - 6 Social isolate, no friends, not even superficial relationships.

3. Scholastic Performance
   - 0 Excellent student.
   - 1
   - 2 Good student.
   - 3
   - 4 Fair student.
   - 5
   - 6 Failing all classes.

4. Adaptation to School
   - 0 Good adaptation, enjoys school, no or rare discipline problems, has friends at school, likes most teachers.
   - 1
   - 2 Fair adaptation, occasional discipline problems, not very interested in school but no/or rare truancy, has friends in school but does not often take part in extracurricular activities.
   - 3

4 Poor adaptation, dislikes school, frequent discipline problem.
5
6 Refuses to have anything to do with school – delinquency or vandalism directed against school.

5. Social-Sexual Aspects of Life During Early Adolescence
   0 Started dating, showed a "healthy interest" in the opposite sex, may have gone "steady," may include some sexual activity.
   1 Attachment and interest in others – may be same sex attachments, may be a member of a group, interested in the opposite sex although may not have close emotional relationship with someone of the opposite sex, "crushes" and flirtations.
   2 Consistent deep interest in same sex attachments with restricted or no interest in the opposite sex.
   3 Casual same-sex attachments with inadequate attempts at relationships with the opposite sex, casual contacts with both sexes.
   4 Casual contacts with the same sex, no interest in the opposite sex.
   5 A loner, no or rare contacts with either boys or girls.
   6 Antisocial, avoids and avoided by peers (differs from above in that an active avoidance of others rather than passive withdrawal is implied).

ADOLESCENCE (LATE, 16-18)

1. Sociability and Withdrawal
   0 Not withdrawn, actively and frequently seeks out social contacts.
   1
   2 Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize.
   3
   4 Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others but does not seek it.
   5
   6 Unrelated to others, withdrawn and isolated, avoid contact.

2. Peer Relationships
   0 Many friends, close relationships with several.
   1
   2 Close relationships with a few friends (one or two), casual friendships with others.
   3
   4 Deviant friendship patterns – friendly with children younger or older only, or relatives only, or casual relationships only.
   5
   6 Social isolate, no friends, not even superficial relationships.

3. Scholastic Performance
   - 0 Excellent student.
   - 1
   - 2 Good student.
   - 3
   - 4 Fair student.
   - 5
   - 6 Failing all classes.

4. Adaptation to School
   - 0 Good adaptation, enjoys school, no or rare discipline problems, has friends at school, likes most teachers.
   - 1
   - 2 Fair adaptation, occasional discipline problems, not very interested in school but no/or rare truancy, has friends in school but does not often take part in extracurricular activities.
   - 3
   - 4 Poor adaptation, dislikes school, frequent discipline problem.
   - 5
   - 6 Refuses to have anything to do with school – delinquency or vandalism directed against school.

5. Social Aspects of Sexual Life During Adolescence and Immediately Beyond
   - 0 Always showed a "healthy interest" in the opposite sex, dating, has gone "steady," engaged in some sexual activity (not necessarily intercourse).
   - 1 Dated regularly, had only one friend of the opposite sex with whom the patient went "steady" for a long time (includes sexual aspects of a relationship, although not necessarily intercourse, implies a twosome pairing off into couples, as distinguished from above).
   - 2 Always mixed closely with boys and girls (involves membership in a crowd, interest in and attachment to others, no couples).
   - 3 Consistent deep interest in same-sex attachments with restricted of no interest in the opposite sex.
   - 4 Casual same-sex attachments with inadequate attempts at adjustment to going out with the opposite sex, casual contacts with boys and girls.
   - 5 Casual contacts with same sex with lack of interest in opposite sex, occasional contacts with the opposite sex.
   - 6 No desire to be with boys and girls, never went out with the opposite sex.

<u>ADULTHOOD (AGE 19 AND ABOVE)</u>

1. Sociability and Withdrawal
   - 0 Not withdrawn, actively and frequently seeks out social contacts.
   - 1
   - 2 Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize.

3

4 Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others but does not seek it.

5

6 Unrelated to others, withdrawn and isolated, avoid contact.

2. Peer Relationships

0 Many friends, close relationships with several.

1

2 Close relationships with a few friends (one or two), casual friendships with others.

3

4 Deviant friendship patterns – friendly with children younger or older only, or relatives only, or casual relationships only.

5

6 Social isolate, no friends, not even superficial relationships.

3. Aspects of Adult Social-Sexual Life

a. Married, presently or formerly

0 Married, only one marriage (or remarried as a result of death of spouse), living as a unit, adequate sexual relations.

1 Currently married with a history of low sexual drive, periods of difficult sexual relations or extramarital affair.

1 Married, more than one time, currently remarried, adequate sexual relations during at least one marriage.

2 Married, and apparently permanently separated or divorced without remarriage, but maintained a home in one marriage for at least three years.

3 Same as above, but divorce occurred over 3 years ago and while married maintained a home for less than 3 years.

b. Never married, over 30

2 Has been engaged one or more times or has had a long-term relationship (at least 2 years) involving heterosexual or homosexual relations, or apparent evidence of a love affair with one person but unable to achieve a long-term commitment such as marriage.

3 Long-term heterosexual or homosexual relationships lasting over 6 months but less than 2 years (if stable, long-lasting homosexual relationship, over 2 years, score as 3).

4 Brief, or short-term dating experiences (heterosexual or homosexual) with One or more partners but no long-lasting sexual experience with a single Partner.

5 Sexual and/or social relationships rare or infrequent.

6 Minimal sexual or social interest in either men or women, isolated.

c. Never married, age 20-29

0 Has had at least one long-term love affair (minimum of 6 months) or engagement even though religious or other prohibitions or inhibitions may have prevented actual sexual union, may have lived together.

1 Has dated actively, had several "boyfriends" or "girlfriends," some relationships have lasted a few months, but no long-term relationships, relationships may have been "serious" but a long-term commitment such as marriage was not understood to be an eventuality.

3 Brief, short-term dating experiences or "affairs" with one or more partners, but no long-lasting sexual experiences with a single partner.

4 Casual sexual or social relationships with persons of either sex with no deep emotional bonds.

5 Sexual and/or social relationships rare or infrequent.

6 Minimal sexual or social interests in either men or women, isolated.

GENERAL

1. Education

0 Completed college and/or graduate school or professional school (i.e. Law).

1 Completed high school and some college or vocational training school or business school (such as secretarial or computer programming school).

2 Completed high school.

3

4 Completed eighth grade.

5

6 Did not get beyond fifth grade.

2. During a period of 3 years up to 6 months before first hospitalization or onset of first episode, patient was employed for pay or functioning in school

0 All of the time.

1

2 Half of the time.

3

4 Briefly, about 25 percent of the time.

5

6 Never.

3. Within a period of a year up to 6 months before first hospitalization or first episode change in work or school performance occurred

0 Abruptly.

1

2 Within 3 months.

3

4 Within 6 months.

5

6 Imperceptibly, difficult or not possible to determine onset of deterioration.

4. During a period of 3 years up to 6 months before first hospitalization or first episode, frequency of job change, if working, or interruption of school attendance

0 Same job held, or remained in school.

1

2 Job change or school interruption occurred two to three times.

3

4 Kept the same job more than 8 months but less than a year, or remained continuously in school for the same period.

5

6 Less than 2 weeks at a job or in school.

5. Establishment of Independence

0 Successfully established residence away from family home, financially independent of parents.

2 Made unsuccessful attempts to establish independent residence, lives in parents home but pays parents room and board, otherwise financially independent.

4 Lives in parents' home, receiving allowance from parents which patient budgets to pay for entertainment, clothes, etc.

6 Made no attempt to leave home or be financially independent.

6. Global assessment of highest level of functioning achieved in patient's life

0 Fully able to function successfully in and take pleasure from 1) school or job, 2) friends, 3) intimate sexual relationships, 4) church, hobbies, etc.; enjoys life and copes with it well.

2 Able to function well in and enjoys some spheres of life but has a definite lack of success in at least one area.

4 Minimum success and pleasure in three areas of life.

6 Unable to function in or enjoy any aspects of life.

APPENDIX D:

THE SCALE FOR THE ASSESSMENT OF NEGATIVE SYMPTOMS

(Andreasen, 1984)

SCALE FOR THE ASSESSMENT OF NEGATIVE SYMPTOMS (SANS)

0=None 1=Questionable 2=Mild 3=Moderate 4=Marked 5=Severe

AFFECTIVE FLATTENING OR BLUNTING

1. Unchanging Facial Expression The patient's face appears wooden – changes less than expected as emotional content of discourse changes.	0 1 2 3 4 5
2. Decreased Spontaneous Movements The patient shows few or no spontaneous movements, does not shift positions, move extremities, etc.	0 1 2 3 4 5
3. Paucity of Expressive Gestures The patient does not use hand gestures, body position, etc., as an aid in expressing his ideas.	0 1 2 3 4 5
4. Poor Eye Contact The patient avoids eye contact or "stares through" interviewer even when speaking.	0 1 2 3 4 5
5. Affective Nonresponsivity The patient fails to laugh or smile when prompted.	0 1 2 3 4 5
6. Inappropriate Affect The patient's affect is inappropriate or incongruous, not simply flat or blunted.	0 1 2 3 4 5
7. Lack of Vocal Inflections The patient fails to show normal vocal emphasis patterns, is often monotonic.	0 1 2 3 4 5
8. Global Rating of Affective Flattening This rating should focus on overall severity of symptoms, especially unresponsiveness, eye contact, facial expression and vocal inflections.	0 1 2 3 4 5

ALOGIA

9. Poverty of Speech The patient's replies to questions are restricted in amount, tend to be brief, concrete, unelaborated.	0 1 2 3 4 5

10. Poverty of Content of Speech
The patient's replies are adequate in amount but tend to be vague, overconcrete or overgeneralized, and convey little information. 0 1 2 3 4 5

11. Blocking
The patient indicates, either spontaneously or with prompting, that his train of thought was interrupted. 0 1 2 3 4 5

12. Increased Latency of Response
The patient takes a long time to reply to questions; prompting indicates the patient is aware of the question. 0 1 2 3 4 5

13. Global Rating of Alogia
The core features of alogia are poverty of speech and poverty of content. 0 1 2 3 4 5

AVOLITION -- APATHY

14. Grooming and Hygiene
The patient's clothes may be sloppy or soiled, and he may have greasy hair, body odor, etc. 0 1 2 3 4 5

15. Impersistence at Work or School
The patient has difficulty seeking or maintaining employment, completing school work, keeping house, etc. If an inpatient, cannot persist at ward activities, such as OT, playing cards, etc. 0 1 2 3 4 5

16. Physical Anergia
The patient tends to be physically inert. He may sit for hours and not initiate spontaneous activity. 0 1 2 3 4 5

17. Global Rating of Avolition - Apathy
Strong weight may be given to one or two prominent symptoms if particularly striking. 0 1 2 3 4 5

ANHEDONIA -- ASOCIALITY

18. Recreational Interests and Activities
The patient may have few or no interests. Both the quality and quantity of interests should be taken into account. 0 1 2 3 4 5

19. Sexual Activity
The patient may show decrease in sexual interest and activity, or enjoyment when active. 0 1 2 3 4 5

20. Ability to Feel Intimacy and Closeness
The patient may display an inability to form close or intimate relationships, especially with opposite sex and family. 0 1 2 3 4 5

21. Relationships with Friends and Peers
The patient may have few or no friends and may prefer to spend all his time isolated. 0 1 2 3 4 5

22. Global Rating of Anhedonia - Asociality
This rating should reflect overall severity, taking into account the patient's age, family status, etc. 0 1 2 3 4 5

ATTENTION

23. Social Inattentiveness
The patient appears uninvolved or unengaged. He may seem "spacey." 0 1 2 3 4 5

24. Inattentiveness during Mental Status Testing
Tests of "serial 7's" (at least 5 subtractions) and spelling "world" backwards. 0 1 2 3 4 5
(score 2 = 1 error, score 3 = 2 errors, score 4 = 3 errors)

25. Global Rating of Attention
This rating should assess the patient's overall concentration, clinically and on tests. 0 1 2 3 4 5

APPENDIX E:

THE SCALE FOR THE ASSESSMENT
OF POSITIVE SYMPTOMS

(Andreasen, 1984)

SCALE FOR THE ASSESSMENT OF POSITIVE SYMPTOMS (SAPS)

0=None 1=Questionable 2=Mild 3=Moderate 4=Marked 5=Severe

HALLUCINATIONS

1. Auditory Hallucinations The patient reports voices, noises, or other sounds that no one else hears	0 1 2 3 4 5
2. Voices Commenting The patient reports a voice which makes a running commentary on his behavior or thoughts.	0 1 2 3 4 5
3. Voices Conversing The patient reports hearing two or more voices conversing.	0 1 2 3 4 5
4. Somatic or Tactile Hallucinations The patient reports experiencing peculiar physical sensations in the body.	0 1 2 3 4 5
5. Olfactory Hallucinations The patient reports experiencing unusual smells which no one else notices.	0 1 2 3 4 5
6. Visual Hallucinations The patient sees shapes or people that are not actually present.	0 1 2 3 4 5
7. Global Rating of Hallucinations This rating should be based on the duration and severity of the hallucinations and their effect on the patient's life.	0 1 2 3 4 5

DELUSIONS

8. Persecutory Delusions The patient believes he is being conspired against or persecuted in some way.	0 1 2 3 4 5
9. Delusions of Jealousy The patient believes his spouse is having an affair with someone.	0 1 2 3 4 5
10. Delusions of Guilt or Sin The patient believes that he has committed some terrible sin or done something unforgiveable.	0 1 2 3 4 5

11. Grandiose Delusions
The patient believes he has special powers or abilities. 0 1 2 3 4 5

12. Religious Delusions
The patient is preoccupied with false beliefs of a religious nature. 0 1 2 3 4 5

13. Somatic Delusions
The patient believes that somehow his body is diseased, abnormal, or changed. 0 1 2 3 4 5

14. Delusions of Reference
The patient believes that insignificant remarks or events refer to him or have special meaning. 0 1 2 3 4 5

15. Delusions of Being Controlled
The patient feels that his feelings or actions are controlled by some outside force. 0 1 2 3 4 5

16. Delusions of Mind Reading
The patient feels that people can read his mind or know his thoughts. 0 1 2 3 4 5

17. Thought Broadcasting
The patient believes that his thoughts are broadcast so that he himself or others can hear them. 0 1 2 3 4 5

18. Thought Insertion
The patient believes that thoughts that are not his own have been inserted into his mind. 0 1 2 3 4 5

19. Thought Withdrawal
The patient believes that thoughts have been taken away from his mind. 0 1 2 3 4 5

20. Global Rating of Delusions
This rating should be based on the duration and persistence of the delusions and their effect on the patient's life. 0 1 2 3 4 5

<u>BIZARRE BEHAVIOR</u>

21. Clothing and Appearance
The patient dresses in an unusual manner or does other strange things to alter his appearance. 0 1 2 3 4 5

22. Social and Sexual Behavior
The patient may do things considered inappropriate according to usual social norms (e.g., masturbating in public). 0 1 2 3 4 5

23. Aggressive and Agitated
The patient may behave in an aggressive, agitated manner, often unpredictable. 0 1 2 3 4 5

24. Repetitive or Stereotyped Behavior
The patient develops a set of repetitive actions or rituals that he must perform over and over. 0 1 2 3 4 5

25. Global Rating of Bizarre Behavior
This rating should reflect the type of behavior and the extent to which it deviates from social norms. 0 1 2 3 4 5

POSITIVE FORMAL THOUGHT DISORDER

26. Derailment
A pattern of speech in which ideas slip off track onto ideas obliquely related or unrelated. 0 1 2 3 4 5

27. Tangentiality
Replying to a question in an oblique or irrelevant manner. 0 1 2 3 4 5

28. Incoherence
A pattern of speech which is essentially incomprehensible at times. 0 1 2 3 4 5

29. Illogicality
A pattern of speech in which conclusions are reached which do not follow logically. 0 1 2 3 4 5

30. Circumstantiality
A pattern of speech which is very indirect and delayed in reaching its goal idea. 0 1 2 3 4 5

31. Pressure of Speech
The patient's speech is rapid and difficult to interrupt; the amount of speech produced is greater than that considered normal. 0 1 2 3 4 5

32. Distractible Speech
The patient is distracted by nearby stimuli which interrupt his flow of speech. 0 1 2 3 4 5

33. Clanging
A pattern of speech in which sounds rather than meaningful relationships govern word choices. 0 1 2 3 4 5

34. Global Rating of Positive Formal Thought Disorder
This rating should reflect the frequency of abnormality and degree to which it effects the patient's ability to communicate.

0 1 2 3 4 5

APPENDIX F:

THE BRIEF PSYCHIATRIC RATING SCALE

(Overall & Gorham, 1962)

THE BRIEF PSYCHIATRIC RATING SCALE

1	2	3	4	5	6	7
not present	very mild	mild	moderate	moderately severe	severe	extremely severe

1. SOMATIC CONCERN _____
Degree of concern over present bodily health. Rate the degree to which physical health is perceived as a problem by the patient, whether complaints have realistic basis or not.

2. ANXIETY _____
Worry, fear, or over-concern for present or future. Rate solely on the basis of verbal report of patient's own subjective experiences. Do not infer anxiety from physical signs or from neurotic defense mechanisms.

3. EMOTIONAL WITHDRAWAL _____
Deficiency in relating to the interviewer and to the interview situation. Rate only the degree to which the patient gives the impression of failing to be in emotional contact with other people in the interview situation.

4. CONCEPTUAL DISORGANIZATION _____
Degree to which the thought processes are confused, disconnected or disorganized. Rate on the basis of integration of the verbal products of the patient. Do not rate on the basis of patient's subjective impression of his own level of functioning.

5. GUILT FEELINGS _____
Over-concern or remorse for past behavior. Rate on the basis of the patient's subjective experiences of guilt as evidenced by verbal report with appropriate affect. Do not infer guilt feelings from depression, anxiety of neurotic defenses.

6. TENSION _____
Physical and motor manifestations of tension, "nervousness," and heightened activation level. Tension should be rated solely on the basis of physical signs and motor behavior and not on the basis of subjective experiences of tension reported by the patient.

7. MANNERISMS AND POSTURING _____
Unusual and unnatural motor behavior, the type of motor behavior which causes certain mental patients to stand out in a crowd of normal people. Rate only abnormality of movements. Do not rate simple heightened motor activity here.

8. GRANDIOSITY _____
Exaggerated self-opinion, conviction of unusual ability or powers. Rate only on the basis of patient's statements about himself, or self in relation to others, not on the basis of his demeanor in the interview situation.

9. DEPRESSIVE MOOD _____
Despondency in mood, sadness. Rate only degree of despondency. Do not rate on the basis of inferences concerning depression based upon general retardation and somatic complaints.

10. HOSTILITY _____
Animosity, contempt, belligerence, disdain for other people outside the interview situation. Rate solely on the basis of the verbal report of feelings and actions of the patient toward others. Do not infer hostility from neurotic defenses, anxiety nor somatic complaints. (Rate attitude toward interviewer under "uncooperativeness.")

11. SUSPICIOUSNESS _____
Belief (delusional or otherwise) that: others have now, or have in the past, malicious or discriminatory intent toward the patient. On the basis of verbal report, rate only those suspicions which are currently held whether they concern past or present circumstances.

12. HALLUCINATORY BEHAVIOR _____
Perceptions without normal external stimulus correspondence. Rate only those experiences which are reported to have occurred within the last week and which are described as distinctly different from the thought and imagery processes of normal people.

13. MOTOR RETARDATION _____
Reduction in energy level evidenced in slowed movements. Rate on the basis of observed behavior of the patient only. Do not rate on the basis of patient's subjective impression of own energy level.

14. UNCOOPERATIVENESS _____
Evidence of resistance. Unfriendliness, resentment, and lack of readiness to cooperate with interviewer. Rate only on the basis of the patient's attitude and responses to the interviewer and the interview situation. Do not rate on basis of reported resentment or uncooperativeness outside the interview situation.

15. UNUSUAL THOUGHT CONTENT _____
Unusual, odd, strange, or bizarre thought content. Rate here the degree of unusualness, not the degree of disorganization of thought processes.

16. BLUNTED AFFECT _____
Reduced emotional tone, apparent lack of normal feeling or involvement.

17. EXCITEMENT _____
Heightened emotional tone, agitation, increased reactivity.

18. DISORIENTATION _____
Confusion or lack of proper association for person, place or time.

APPENDIX G:

CONSENT FORM

University of Pennsylvania
A Neurobehavioral Study of Schizophrenia: Protocol #782-0
Initial Evaluation and Follow-up Evaluation Consent Form
Neuropsychiatry

Dr. Raquel Gur (215) 662-2826
Dr. Christian Kohler (215) 662-7388
Dr. Bruce Turetsky (215) 662-6094
Dr. Stephen Kanes (215) 662-7388
Dr. Steven Siegel (215) 662-7388
24-hour Emergency (215) 662-6059
(ask for Psychiatry Resident on call)

CONSENT FORM
INITIAL/FOLLOW-UP EVALUATION

SELECTION OF SUBJECTS

Our research center is dedicated to the study of brain function in healthy people and people with brain disorders. We evaluate individuals and their family members in order to get comprehensive information

You were selected because you are:
_____ a healthy control subject
_____ a family member subject
_____ a subject with a brain disorder
_____ a healthy pregnant woman
_____ a pregnant woman with a brain disorder

and you are willing to participate in research on brain processes and behavior and you have met other inclusion criteria. These inclusion criteria are based on medical and design requirements, and do not discriminate on the basis of sex or ethnic background.

PURPOSE

The purpose of conducting these research studies is to learn about how the brain works. This is done by studying patients with brain disorders and their relatives and comparing these results with healthy people and their relatives who do not. In addition, the relationship between brain abnormalities in the patients and the risk for psychiatric disorder in their relatives is being assessed. This may help to learn more about genetic factors that are important in brain function and disease. Before participating in any specific study we need to evaluate your health status.

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PROCEDURE

Initial Evaluation

The first step is a standard clinical interview followed by personality questionnaires. You will be given a medical evaluation which includes a history, physical examination, and routine laboratory tests. The tests consist of urine and blood tests. For the blood tests, approximately 40ml (about 2.5 tablespoons) of your blood will be needed. If you are a female, an additional 20ml of blood may be drawn at the same time to examine hormone levels.

You agree to have a sample of blood taken for genetic studies. The blood cells will be transformed to allow them to be stored permanently or grown in culture for long periods. Transformation allows many genetic measures to be made on a very small sample of blood. The amount of blood obtained will be approximately 40ml (about 2.5 tablespoons). The procedure involves placing a needle in a vein in your arm to take blood.

If you are a female, you may be asked to keep track of your menstrual cycle for approximately 3 months using a diary or a calendar. We may contact you by phone periodically to remind you about the diary. Your medical evaluation which includes a health history will place special emphasis on menstruation.

If you are pregnant we will ask you questions about the pregnancy and how you are doing and will work with the doctors in the obstetric clinic to get information about your health and the development of the baby.

Follow-Up Evaluation

We have a particular interest in the changes which occur in brain function over time and we shall contact you again in the future to ask if we can repeat some of the investigations. At follow-up, you will be asked questions about how things have been going for you since your initial evaluation and you may be asked to repeat studies or to participate in new studies.

If you are a female, you may be asked to keep track of your menstrual cycle for approximately 3 months using a diary or a calendar. We may contact you by phone periodically to remind you about the diary. Your medical evaluation which includes a health history will place special emphasis on menstruation.

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If you are pregnant, we would like to see you when you come for your obstetrical visit about once a month. We will check how you are doing and get information from your doctors in the obstetric clinic about your health and the development of the baby. This will continue during the pregnancy. At the time of delivery we will check how you are doing and how the baby is doing and again will like to get information from the doctors who take care of you and the baby.

RISKS

Occasionally there are minor complications, and you may experience bruising, swelling and/or black and blue marks at the site. Should you develop any complications, you should call Dr. Raquel Gur at her office (662-2826 or 662-2915) or by pager (452-4745) or one of the other doctors listed on this consent form. Should you be unable to reach Dr. Gur or any other physician associated with the study, you should go to the emergency room of the Hospital of the University of Pennsylvania. You will receive a copy of this consent form, which contains the procedures to be followed in case any complications occur.

BENEFITS

Although the results of this evaluation may not benefit you directly, they can easily be made available to your physician upon request.

ALTERNATIVES

The alternative to this study is not to participate.

COMPENSATION

You will be reimbursed for your travel and parking expenses.

CONFIDENTIALITY

Data collected during this evaluation will be confidential, except as may be required by law and any publication resulting from the research will not personally identify you.

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DISCLAIMER/WITHDRAWAL

You understand that you are free to decide whether or not to participate and to withdraw from the study at any time. You are assured that if you withdraw from this project this will not influence standards of care or services provided to you by the participating facilities.

INJURY/COMPLICATIONS

You understand that in the event of injury resulting from the research procedures, medical treatment in excess of that covered by third party payors will be provided without cost to you, but financial compensation for injury is not available.

SUBJECT RIGHTS

You understand that if you wish further information regarding your rights as a research subject, you may contact the Director in the Office of Regulatory Affairs at the University of Pennsylvania by telephoning (215) 898-2614. You also understand that if you have any questions pertaining to your participation in this research study you may contact the physician by calling the telephone number(s) listed at the top of page one. You have been given the opportunity to ask questions and have had them answered to your satisfaction.

CONCLUSION

You have read and received a copy of this consent form and have been given the opportunity to ask questions. You realize this consent is voluntary and may be withdrawn at any time without prejudicing your care.

You agree to participate in this study voluntarily.

_____ _____
Subject's Signature Date

_____
Subject's Name (print)

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Neuropsychiatry

_____	_____
Signature of Witness	Date
_____	
Name of Witness (print)	
_____	_____
Signature of Investigator	Date

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