Significance of the Positive-Negative Distinction in Schizophrenia

by Stanley R. Kay

Abstract

This article reviews the cumulative research on positive and negative syndromes in schizophrenia undertaken at the Albert Einstein College of Medicine. A strictly operationalized and standardized syndrome scale was applied in multidimensional, cross-sectional, prospective, longitudinal, phasic, and drug-free studies. The following conclusions about positive and negative syndromes were reached: they can be reliably assessed; they are normally distributed and theoretically independent, thus representing dimensions rather than coexclusive subtypes of schizophrenia; they differ in their association with premorbid functioning, family history of illness, cognitive profile, and neurological signs; their significance appears phase-specific, however, with ominous implications for a negative syndrome found only in the chronic stage; their magnitude is comparably high in all stages of the illness, challenging the view of a progressive negative state; they are stable under drug-free conditions and across months of drug therapy; they both improve with neuroleptics, with marginally better response for positive syndrome; worse long-range outcome is predicted by positive syndrome, especially by disorganized thinking, whereas worse short-term outcome is predicted by both syndromes; the positive-negative distinction, though valid, is incomplete as a model of schizophrenic phenomenology, which must include unrelated depressive and excited components; and Kraepelinian subtypes of schizophrenia seem to comprise not single pathological processes but a hybrid of unrelated, co-occurring syndromes.

Schizophrenia, after decades of research, remains one of the most enigmatic and devastating of the psychiatric disorders. Its resistance to scientific study seems to be rooted in its elusive nature. Since the early writings of Bleuler (1911/1950) almost 80 years ago, it has been recognized that schizophrenia is a heterogeneous condition, and any attempt to understand it requires explanation of its various guises or components. Clearly, schizophrenic patients differ widely in their symptomatic presentation, premorbid functioning, genetic liability, response to medication, and prognosis.

Such diversity raises serious doubt about the efficacy and even the logic behind our principal treatment for schizophrenia, the neuroleptic drug. The use of dopamine blocking agents, which originated in the 1950's, best fits a unitary model of schizophrenia, one characterized by an excess of the neurotransmitter dopamine. The limitation of this treatment is revealed, however, in its lack of efficacy for a large segment of patients and in its failure to reverse many crucial symptoms, even among those patients who are capable of hospital discharge.

The need for a revised and expanded view of schizophrenia has, therefore, become increasingly apparent. One major advance in the past decade has come from Crow's (1980a, 1980b) proposal that two separate symptom profiles may be recognized in schizophrenia. He hypothesized that positive or productive symptoms prevail in the acute stage and may represent hyperdopaminergia. Patients of this type were...
thus characterized by a neurochemical abnormality that is considered reactive to neuroleptics and portends a good outcome. Negative or deficit symptoms, by contrast, were thought to predominate mainly in the chronic stage and to signify structural brain abnormality, such as indicated by ventricular enlargement. Patients of this description were expected to be neuroleptic resistant and to carry a poor prognosis.

As noted by lager et al. (1985), negative or deficit features of mental illness were identified by Pinel as long ago as 1801. The origins of the positive-negative terminology are usually attributed to Hughlings Jackson (1887), who drew the distinction not to describe unrelated symptoms but, rather, to delineate primary from secondary neurological phenomena. Although not employing this terminology, Bleuler (1911/1950) and Kraepelin (1919/1971) provided a conceptual framework for its current application to schizophrenia by describing symptom complexes that today would be recognized as positive or negative clusters. The empirical roots of the positive-negative distinction, however, owe much to the factor analytic studies of the 1960’s and, particularly, to the research of Strauss et al. (1974), who adapted Jackson’s terminology for classifying different profiles in schizophrenia.

Whereas Crow’s (1980a, 1980b) seminal model viewed the positive and negative symptoms as unrelated facets of schizophrenia that reflect separate pathological processes, Andreasen (Andreasen and Olsen 1982; Andreasen et al. 1982) initially proposed that these symptoms represent opposing features that characterize different subtypes. More recently, Carpenter and colleagues have argued that negative symptoms do not form a unitary construct and, hence, that a more meaningful concept is one of deficit syndrome, which would additionally denote intractability over a period of time (Carpenter et al. 1985, 1988).

Although the viewpoint on positive and negative symptoms has thus spawned rival models, the distinction retains obvious appeal both in its simple dichotomization rooted in different forms of neuropathology and in its embrace of much of the diversity seen in schizophrenia. If validated, this approach would constitute a milestone in clarifying systematic differences in the etiology, pharmacotherapy, and prognosis of schizophrenia.

The empirical research, unfortunately, has not uniformly supported the principal tenets of the positive-negative distinction (cf. Pogue-Geile and Zubin 1988). Critical inspection of the experiments by Angrist et al. (1980) and Andreasen and Olsen (1982), which are often quoted to support the validity of this distinction, has revealed inadequacies in the sampling and results that undermine the interpretations given (Opler et al. 1987). For example, Andreasen’s negative schizophrenia group was significantly older than the positive one and had far more experience with electroconvulsive treatment (56% vs. 5%), which might well account for some of the cognitive and neurological differences. In the Angrist study, the conclusion that negative symptoms failed to respond to neuroleptics is compromised by the fact that one of the three negative items (emotional withdrawal) did, indeed, improve significantly. Subsequent studies on the relationship of negative symptomatology to brain structure, drug response, phase of illness, and prognosis have yielded mixed results that defy simple categorization (see review by Pogue-Geile and Zubin 1988).

**Limitations in Methodology**

The lack of consistency in findings, however, is not a conclusive reason to discount the validity of the positive-negative distinction. It has been noted that this still young area of research is beset by fundamental weaknesses in the methodology that are likely to augment Type II error—that is, to mitigate against consistent findings (Sommers 1985; Zubin 1985; Kay and Opler 1987).

First is the reliance on scales that are not fully operationalized and standardized, thus promoting measurement that is weak, inaccurate, or simply invalid. For example, the generally used scales (e.g., Overall and Gorham 1962; Andreasen and Olsen 1982; Lewine et al. 1983; Heinrichs et al. 1984; lager et al. 1985) provide neither a standardized interview nor specific rating criteria to decide between different levels of symptom severity, such as mild versus moderate (see review by Kay, in press). These methods also have been criticized for uncertain content and construct validity as well as for lack of retest reliability (Zubin 1985; Kay et al. 1986b; Liddle 1987b). Carpenter et al. (1985) persuasively argued that several of the symptoms that have been classified as negative (e.g., attention dysfunction and disorientation) may actually be secondary to positive features, such as hallucinations and hyperarousal. The research at Columbia University (Bilder et al. 1985; Cornblatt et al. 1985) and at our own facility (Kay et al. 1986a, 1986c) confirms that an attentional impairment, for instance, clusters equally with negative and positive phenomena.
Second, it is noteworthy that many studies analyze the negative syndrome in a vacuum, without due consideration for how it may differ from the positive syndrome, depression, or other facets of the illness. Unless the significance attributed to the negative syndrome is particular to that cluster of symptoms, the conclusions will be grossly misleading, having perhaps more to do with the severity than the character of the disorder. Studies on negative psychopathology, therefore, require a psychometrically comparable measurement of other symptoms that serve, in effect, as "controls" to provide this relational perspective.

A third concern is the tendency to study syndromes cross-sectionally. The popularity of cross-sectional designs could have much to do with their congeniality for quick and large-scale data collection. It is important to recognize, however, that the cross-sectional view is a static one that tells us little about hypothesized processes and, by its very nature, precludes inspection of their stability, course, and mutability over time. Since the negative syndrome has been ascribed specific longitudinal characteristics—prominence in the chronic stage, lack of response to neuroleptics, poor outcome, and (by implication) stability over at least brief periods—it is essential that studies of its validity be able to test these assumptions.

Fourth, the relatively few investigations that examine positive and negative syndromes longitudinally seem only to apply either a short-term design that covers several weeks of neuroleptic treatment or a retrospective view of the course of illness. For example, the longitudinal studies of Pogue-Geile and Harrow (1984, 1985), though highly informative, were derived from retrospective assessment of symptoms rather than from concurrent baseline analysis and subsequent followup. Without a prospective design we cannot establish the predictive significance of a positive or negative presentation, and without long-term followup we cannot presume to know the prognostic import of such a presentation.

Fifth, most studies of these phenomena use either a sample in the advanced phase of illness or one that is heterogeneous with respect to chronicity. To consider whether the meaning of the positive-negative distinction is constant across the course of illness, it is important to study clearly defined, homogeneous samples at different stages (e.g., acute, subacute, chronic).

Sixth, the overwhelming majority of studies on these syndromes have not investigated patients in the drug-free state. As a result, the observations may be contaminated by prior clinical response to neuroleptics, which will obviously alter the psychiatric picture in specific ways. The very persistence of positive or negative features after drug treatment may, in fact, provide for a self-selected sample in studies that lack a drug-free baseline. Thus, one cannot reasonably assume that the negative profile carries the same meaning in a drug-treated patient as in an unmedicated one whose negative symptoms have gone unchallenged and, therefore, may still subside with the intervention.

Furthermore, as has been amply stressed (Rifkin et al. 1975; Carpenter et al. 1985), the assessment of negative symptoms in medicated patients may be confounded by extrapyramidal side effects (EPS) that restrict verbal, motor, and social functions.

Mindful of these methodological pitfalls, our research group has embarked on studies aiming for a sharper and fuller perspective on the validity and significance of the positive-negative distinction in schizophrenia. Our strategy has involved use of a well-operationalized syndrome scale, large-scale and multidimensional assessment, longitudinal study with prospective baseline measures, and either a drug-free evaluation or independent control ratings of drug side effects. It will be seen that the cumulative findings support the reliability and validity of the negative syndrome in schizophrenia as a pathological process distinct from the positive syndrome, depression, EPS, and general psychopathology. The significance of the positive-negative distinction, however, does not conform to the models originally proposed by Crow and Andreasen. These syndromes seem to differ systematically at different stages of the illness and, alone, are insufficient to explain the full range of schizophrenic phenomena.

New Assessment Method

It is axiomatic that the validity and scope of one's observations are directly limited by the validity and scope of the device used for measurement. This is particularly true in studying a new construct, such as positive and negative syndromes (Zubin 1985). For this reason, and in light of the limitations of the existing instruments, we developed and standardized a psychiatric rating scale in accordance with the guidelines for test construction mandated by the American Psychological Association (1985). The result is the 30-item, 7-point Positive and Negative Syndrome Scale (PANSS; Kay et al. 1987a), which has the following psychometric advantages: (1) formal
criteria for conducting the 30- to 40-minute psychiatric interview, which follows a four-stage sequence for comprehensive assessment; (2) thorough definition of all items at each of seven levels of symptom severity, as contained in the PANSS Rating Manual (Kay et al., in press); (3) standard videotape procedure for training in the PANSS interview and ratings (Kay 1989a) to help establish consensus across raters and research centers; (4) content sampling that is balanced, encompasses several functional spheres, and excludes from the negative scale items elsewhere found to correlate with positive features (e.g., poor attention and disorientation); (5) measurement of positive syndrome, negative syndrome, depression, and general psychopathology to serve as bases for comparison; (6) normative data on 240 schizophrenic patients to assist in empirical screening decision rules and score interpretation; and (7) translation into 15 languages, which can foster multinational and cross-cultural study.

Although the rating points for each symptom are separately defined, the judgment of severity ("absent" to "extreme") across items is key to the prominence of manifestations, their frequency, and their disruptive impact on daily life functions. The seven positive items are delusions, conceptual disorganization, hallucinatory behavior, excitement, grandiosity, suspiciousness/persecution, and hostility. The seven negative items are blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, and stereotyped thinking. Another 16 items that cannot be definitively classified as positive or negative constitute a general psychopathology scale. The positive, negative, and general psychopathology scores are obtained by summing ratings across the component items, which yields respective ranges of 7-49, 7-49, and 16-112. Depression is also assessed, as per the Brief Psychiatric Rating Scale (BPRS) cluster (Guy 1976), by summing items of depression, guilt feelings, anxiety, and somatic concern.

The positive and negative items were selected for consistency with Crow's (1980a, 1980b) Type I-Type II concept, syndrome specificity, and broad representation of symptoms from the cognitive, social, emotional, and communicational realms. As a result, the scale composition differs from that of other frequently used methods, a point that we have elsewhere elaborated on (Kay, in press) and that could well underlie differences in findings. For example, in comparison with the PANSS, Andreasen and Olsen's (1982) negative scale includes poor attention while excluding conceptual and communicational deficits, and her positive scale excludes symptoms of hyperactivity/excitement, grandiosity, suspiciousness/persecution, and hostility/irritability. The procedure used by Crow, which was developed as a brief, rapid screening device and standardized on "10 known psychiatric patients" (Krawiecka et al. 1977), is limited to only three positive symptoms (delusions, hallucinations, and incoherence or irrelevance of speech) and three negative symptoms (poverty of speech, flattened affect, and psychomotor retardation), of which the latter present modest interrater reliability (mean Kendall $W = 0.64$) and may reflect depressive features. The BPRS (Overall and Gorham 1962) also contains only three negative items (emotional withdrawal, blunted affect, and motor retardation) which, as already noted, seem to respond differentially to neuroleptics (Angrist et al. 1980).

The psychometric properties of the PANSS were studied on a total of 240 schizophrenic patients to evaluate the scale's reliability, validity, and scaling characteristics (Kay et al. 1988, 1989b). On a sample of 31 acute schizophrenic patients, we found the interrater reliabilities between psychiatrist and psychologist to range between 0.81 and 0.88 ($p < 0.0001$). On a sample of 49 chronic schizophrenic patients, we compared our method with that of Andreasen and Olsen (1982) and also against the Clinical Global Impressions scale (Guy 1976). The corresponding Pearson correlations with positive, negative, and general psychopathology scores were 0.78, 0.73, and 0.54, respectively, with $p < 0.0001$ in all cases, supporting the criterion-related validity of the PANSS.

Finally, we examined the internal consistency, distribution, and interrelationships of the PANSS scales on 101 chronic schizophrenic patients (Kay et al. 1987a). Coefficient alpha was 0.83 and 0.73 for the negative and positive scales, respectively, and each of the individual items correlated significantly with the remaining scale total. The three PANSS scales were found to be normally distributed, without substantial skewness or kurtosis, which suggests that they depict typical continua and may be analyzed by parametric statistics. When partialing out the mutual contribution from general severity of illness, positive and negative syndromes appeared to comprise nonoverlapping, discrete aspects of the schizophrenic disorder ($r = -0.23$).
Typological and Dimensional Studies

With the PANSS, we set out to assess the significance of positive and negative syndromes as viewed typologically (as coexclusive subtypes) and dimensionally (as facets that present in varying degrees).

Typological studies were performed separately for 37 acute (Lindenmayer et al. 1984) and 47 chronic schizophrenic inpatients (Opler et al. 1984), so diagnosed by DSM-III criteria (American Psychiatric Association 1980). In both studies, negative patients (defined by a rating of 4 ["moderate"] or higher on at least three of the seven negative items but on fewer than three of the seven positive items) were characterized by poorer education, which suggests a premorbid cognitive liability. The chronic sample, selected for having more than 2 years of illness, was administered the Cognitive Diagnostic Battery (Kay 1982); this consists of five tests that use a Piagetian developmental framework to measure maturation and to delineate it from other cognitive pathology in schizophrenia. Patients who had been grouped as predominantly negative demonstrated a significantly greater deficit on this battery.

The typological studies indicated, however, that (1) only a minority of acute and chronic schizophrenic patients could be classified as predominantly positive (24% and 21%, respectively) or negative (22% and 17%, respectively), and (2) the positive and negative scores were independent rather than coexclusive. This would suggest that the constructs are better conceptualized as separate yet co-occurring dimensions and not as distinct subtypes. Therefore, our next study, involving 101 chronic inpatients with a DSM-III diagnosis of schizophrenia, looked at the syndromes dimensionally (Kay et al. 1986c). The dependent variables encompassed demographic, historical, family history, clinical, psychometric, and extrapyramidal measures. Analyses included both simple and partial correlations that controlled statistically for the modest correlation in this study between negative syndrome and age (r = 0.25) and EPS (r = 0.26). Little difference was obtained from these two methods of analysis (Kay et al. 1986c).

We found the two syndromes to be distinguished by a specific pattern of premorbid, familial, and cognitive deficits. In all respects, the negative syndrome reflected a more pernicious disease process, one that seemed to devolve from probable genetic and developmental sources. It alone was significantly related to less education, lower verbal IQ, and more primitive cognitive functioning on three developmentally based tests from the Cognitive Diagnostic Battery. The negative scale was also significantly associated with a family history of probable schizophrenia—that is, with major psychosis requiring hospitalization and with an absence of affective illness. On the other hand, the positive scale was significantly correlated with sociopathy in first-degree relatives, as inferred from records of criminal conviction. Despite these differences, both syndromes were unrelated to such control variables as race, cultural group, marital status, and age first hospitalized. Contrary to Crow’s (1980a) hypothesis, no differences were found with regard to duration of illness and to global measures of neuropsychological deficit—namely, the Memory-for-Designs Test (Graham and Kendall 1960) and the Progressive Figure Drawing Test (Kay 1980).

Multiple regression analysis indicated that the positive syndrome was best predicted by a wealth of psychopathology, most notably bizarre thinking and angry emotional tone, as well as by a family history of sociopathy or criminality. The negative syndrome was instead predicted by impoverished cognitive and affective processes, deficits in social functioning and cognitive growth, and family history of major psychiatric disorder (Kay et al. 1986c).

Further Cognitive Study

The findings thus far revealed cognitive impairment to be a key distinguishing feature between positive and negative syndromes. Since the negative assessment included difficulty in abstract thinking, however, it was necessary to examine the cognitive processes in greater detail to ensure that our observations were not purely tautological. In addition, although the work reviewed so far found no special neuropsychological liability associated with a negative syndrome, it remained possible that a more localizing or specialized battery would reflect the structural deficits postulated by Crow (1980a).

In subsequent studies, therefore, we examined positive and negative syndromes in relation to specific neurological signs and information-processing disorders. Twenty-eight chronic schizophrenic patients were assessed independently on the PANSS and on a multi-item neurological battery that combined to produce five uncorrelated scores: prefrontal, praxis, parietal, fine motor, and nonlocalizing (Merriam et al., in press). Whereas the PANSS positive syndrome was unrelated to all five scores, the negative syndrome was distinguished by its significant corre-
lation with prefrontal signs \((r = 0.49, p < 0.01)\) but with none of the other neurological variables.

In terms of information processing, we administered three procedures that used techniques from experimental psychology. First, in a sample of 45 schizophrenic patients, we assessed speed of visual processing using the backward masking paradigm with tachistoscopic exposure (Weiner et al., in press). Second, in a sample of 30 schizophrenic patients, we obtained measurements from the Span of Attention Test (SOA; Kay and Singh 1974), which provides a behavioral sampling of concentration on a routine motor task, and on verbal encoding from the Memory Organization Test (MOT; Kay et al. 1989a). The latter uses category clustering in free recall as a vehicle to determine whether the conceptual, affective, or phonemic properties of words are registered.

The results indicated that schizophrenic patients with a pronounced negative syndrome (i.e., > 75th percentile in relation to PANSS norms for schizophrenia) were significantly slower in information processing than other patients and normal controls (Weiner et al., in press). Not only the speed of processing but also the selectivity of stimuli seemed to be deviant. Although a negative syndrome did not entail poorer scores on the SOA attention and the MOT general recall, it was significantly associated with a specific deficiency in encoding the affective connotation of words (Kay et al. 1989a). This might suggest that, beyond their well-known impact on emotional expression (i.e., output), the affective deficits that characterize the negative presentation also have a more fundamental impact on the very process of registering affective cues from the milieu (i.e., input).

Across these studies, therefore, we observed that a negative syndrome was related to measures of prefrontal deficit, cognitive developmental failure, slower information processing, and poorer encoding of affective attributes.

### Longitudinal Course of the Syndromes

Our next strategy involved prospective longitudinal studies to assess the stability and prognostic import of positive and negative syndromes. The PANSS was applied to 37 young acute schizophrenic patients, ages 18–34, who had been newly admitted to an intake unit of an urban psychiatric hospital. All patients had 2 or fewer years duration since their first psychiatric admission (mean = 1.42), and approximately 60 percent had no or only one prior hospitalization. The baseline data indicated that negative symptoms were as prevalent as positive symptoms and did not covary with prolonged institutionalization, general severity of illness, neuroleptic dose, or drug side effects.

It was possible to follow up 19 patients from this sample for an average period of 2.2 years, reflecting on the progression from the acute into the early chronic phase of schizophrenia (Lindenmayer et al. 1986). The followup evaluations were conducted by investigators who were blind to the positive-negative ratings at index admission. A comparison of this group with the dropouts \((n = 18)\) suggested their similarity, since no significant differences were found in age, sex, ethnic group, marital status, education, premorbid ratings, age first hospitalized, or baseline severity of illness \((p \text{ range } 0.15 \text{ to } 0.90)\). When we examined the longitudinal course of the negative and positive syndromes over 2 years, we found no measurable increase or decrease in means and nonsignificant autocorrelations from baseline to followup (see table 1). These observations on acute schizophrenic patients sharply contrasted with those ob-

### Table 1. Stability of negative, positive, and general psychopathology ratings in acute schizophrenic patients from baseline to 2-year followup \((n = 19)\)

<table>
<thead>
<tr>
<th>Phase of study</th>
<th>Negative syndrome</th>
<th>Positive syndrome</th>
<th>General psychopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean score ± SD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline assessment</td>
<td>22.05 ± 7.81</td>
<td>17.26 ± 5.30</td>
<td>2.44 ± 0.78</td>
</tr>
<tr>
<td>Followup assessment</td>
<td>21.16 ± 6.94</td>
<td>18.37 ± 5.45</td>
<td>2.41 ± 0.58</td>
</tr>
<tr>
<td>Change</td>
<td>0.89</td>
<td>-1.11</td>
<td>0.03</td>
</tr>
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</table>

| Statistical test        |                   |                   |                         |
| Paired \(t\)            | 0.36 (NS)         | 0.65 (NS)         | 0.03 (NS)               |
| Pearson \(r\)           | -0.13 (NS)        | 0.24 (NS)         | -0.18 (NS)              |

*Note.—PANSS = Positive and Negative Syndrome Scale.*

*Source.—Based on Lindenmayer et al. (1986).*
tained from patients in the subacute (Kay and Singh 1989) and the chronic phases (Kay et al. 1987a), suggesting greater instability during the early period of illness.

The import of the syndromes, however, seemed to change radically over this transitional phase (table 2). Contrary to popular belief, the negative syndrome at index admission predicted not worse but better subsequent functioning. This was indicated by significant correlations with followup assessments on the 9-item Strauss and Carpenter (1972) Multidimensional Outcome Scale (MOS), which probes social, occupational, and psychiatric adjustment. Some of the predictive correlations were remarkably high—for example, a Pearson $r$ of 0.73 between baseline negative syndrome and followup quantity of useful work. A positive syndrome, meanwhile, carried no prognostic significance. When reassessed 2 years later, however, both syndromes reflected greater severity of the concurrent illness (see table 2).

Although these data support the predictive validity of a negative syndrome in acute schizophrenia, they do not, of course, imply that this clinical variable fully or uniquely explains outcome. As expected, premorbid adjustment, a long-established prognosticator for schizophrenia (Phillips 1953), also showed sizable correlations with overall level of functioning ($r = 0.47, p < 0.05$) and lower general psychopathology ($r = 0.54, p < 0.02$) at 2-year followup. The premorbid functioning, however, was found to be unrelated to negative syndrome ($r = -0.25$). Because of their independence, these predictors combined to produce significantly stronger multiple correlations with the two outcome measures ($r = 0.77, p < 0.001$ and $r = 0.70, p < 0.005$, respectively) (Kay and Lindenmayer 1987).

A parallel longitudinal study was recently completed on a sample of 58 chronic schizophrenic patients drawn from long-term units of the same psychiatric hospital (Kay and Murrill 1990). It was possible to relocate 46 of these patients (79.3%) for followup after a period that averaged 2.7 years. This group was almost 10 years older than our acute sample (mean = 33.1 years) and had a mean of 11.8 years of illness since onset. The dropouts from followup did not differ significantly from the relocated patients in terms of any of

### Table 2. Predictive and contemporaneous significance of negative and positive syndromes in acute schizophrenia ($n = 19$)

<table>
<thead>
<tr>
<th>Outcome criteria</th>
<th>Baseline (predictive $r$)</th>
<th>Followup (contemporaneous $r$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative score</td>
<td>Positive score</td>
</tr>
<tr>
<td>Multidimensional Outcome Scale</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of nonhospitalization</td>
<td>0.53$^2$</td>
<td>-0.13</td>
</tr>
<tr>
<td>Frequency of social contacts</td>
<td>0.39</td>
<td>0.04</td>
</tr>
<tr>
<td>Quality of social relations</td>
<td>0.46$^2$</td>
<td>0.02</td>
</tr>
<tr>
<td>Quantity of useful work</td>
<td>0.73$^5$</td>
<td>0.26</td>
</tr>
<tr>
<td>Quality of useful work</td>
<td>0.61$^4$</td>
<td>-0.09</td>
</tr>
<tr>
<td>Absence of symptoms</td>
<td>0.48$^2$</td>
<td>-0.08</td>
</tr>
<tr>
<td>Ability to meet own basic needs</td>
<td>0.29</td>
<td>0.17</td>
</tr>
<tr>
<td>Fullness of life</td>
<td>0.59$^4$</td>
<td>0.05</td>
</tr>
<tr>
<td>Overall level of functioning</td>
<td>0.47$^2$</td>
<td>0.04</td>
</tr>
<tr>
<td>PANSS general psychopathology</td>
<td>-0.30</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Note.—PANSS = Positive and Negative Syndrome Scale.

$^1$Test of significance of the difference between correlation coefficients for correlated samples.

$^2p < 0.05.$

$^3p < 0.02.$

$^4p < 0.01.$

$^5p < 0.001.$

Source.—Based on Lindenmayer et al. (1988).
The followup assessments, again conducted blindly with respect to baseline data, yielded contrasting conclusions about prognosis as compared with the acute sample. The PANSS negative syndrome in the chronic stage did not significantly predict better or poorer outcome on the MOS. The positive syndrome, however, now carried ominous implications for subsequent functioning on three of the component scales: duration of nonhospitalization ($r = -0.37, p < 0.01$), quantity of useful work ($r = -0.30, p < 0.05$), and fullness of life ($r = -0.33, p < 0.025$). In addition to the rated assessment, the positive syndrome predicted a greater number of days of actual inpatient hospitalization during the followup term ($r = 0.35, p < 0.025$). The general psychopathology scale, like the negative scale, did not significantly predict any of the 10 outcome variables in the 2.7-year followup of this chronic sample.

Multiple regression analysis revealed that 9 of the 10 outcome measures could be reliably predicted by a combination of PANSS clusters, age, years of illness, and family psychiatric history, with multiple $R$ values ranging from 0.49, $p < 0.01$ (for days subsequently hospitalized) to 0.61, $p < 0.0002$ (for fullness of life and ability to meet own basic needs). Of the various clinical clusters measured prospectively on the PANSS, thought disturbance stood out as the single most robust predictor of poor outcome, subsuming most of the predictive variance from the positive syndrome. Alternatively, the depression cluster was the only clinical variable to forecast good outcome and also accounted for a large share of the predictive variance. In predicting duration of nonhospitalization and fullness of life, for example, thought disturbance accounted for 15 percent and 13.7 percent of the variance, respectively, and depression for 11.2 percent and 21.4 percent, while neither the positive nor negative syndrome contributed to the predictions.

The present observations are consistent with recent findings that disorganized thinking may constitute a separate component within the positive syndrome (Bilder et al. 1985; Liddle 1987b), one that portends a poorer functional recovery (Liddle 1987b). Likewise, our data suggest that depression in schizophrenia is clearly distinguishable from the negative syndrome and forms an opposing pole with thought disturbance along the prognostic axis.

**Phasic Studies of the Syndromes**

Despite the methodological strengths of the longitudinal research design, two shortcomings are characteristic: attrition of subjects, which may affect both the sample size and its representation, and limited length of followup that is feasible. For these reasons, we also pursued a cross-sectional approach for a large-scale phasic study of positive and negative syndromes (Kay et al. 1986a). The investigation involved 134 schizophrenic inpatients ages 18-68 (mean = 33.5) who, as per the convention of Brown (1960) and others, were classified according to three stages of the illness: acute (up to 2 years since first hospital admission; mean = 0.61, $n = 33$), chronic (3-10 years; mean = 6.13, $n = 38$), and long-term chronic (longer than 10 years; mean = 19.78, $n = 63$).

In this study, again, we found no difference in the magnitude of syndrome scores as a function of chronicity, suggesting that there is no evolution toward a greater negative presentation. As shown in table 3, both the negative and positive syndrome scores on the PANSS were strikingly similar for the three schizophrenic populations.

Also in keeping with our longitudinal data, the present study found that the significance of the syndromes was stage specific (table 4). In acute schizophrenia, a negative score correlated with familial and

**Table 3. Comparison of negative and positive syndrome scores in acute, chronic, and long-term chronic schizophrenic inpatients**

<table>
<thead>
<tr>
<th>PANSS</th>
<th>Negative (Mean ± SD)</th>
<th>Positive (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenic group</td>
<td>$n$</td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>33</td>
<td>21.42 ± 7.16</td>
</tr>
<tr>
<td>Chronic</td>
<td>38</td>
<td>21.22 ± 5.47</td>
</tr>
<tr>
<td>Long-term chronic</td>
<td>63</td>
<td>21.27 ± 6.19</td>
</tr>
</tbody>
</table>

ANOVA

<table>
<thead>
<tr>
<th>$F$</th>
<th>$p$</th>
</tr>
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<tbody>
<tr>
<td>&lt; 1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>0.99</td>
<td>0.37</td>
</tr>
</tbody>
</table>

Note.—PANSS = Positive and Negative Syndrome Scale. ANOVA = analyses of variance.

Source.—Based on Kay et al. (1986a).
Table 4. Covariates of negative and positive syndromes according to chronicity of illness and tests of significance of the differences

<table>
<thead>
<tr>
<th>Variables</th>
<th>Partial correlation (r)</th>
<th>Difference between rs (z)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acute</td>
<td>Chronic</td>
</tr>
<tr>
<td>Negative syndrome with</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Familial psychosis</td>
<td>-0.30</td>
<td>0.09</td>
</tr>
<tr>
<td>Years of education</td>
<td>-0.24</td>
<td>-0.13</td>
</tr>
<tr>
<td>Guilt feelings</td>
<td>-0.17</td>
<td>-0.44</td>
</tr>
<tr>
<td>Mannerisms and posturing</td>
<td>0.25</td>
<td>-0.25</td>
</tr>
<tr>
<td>Disorientation</td>
<td>0.55</td>
<td>0.24</td>
</tr>
<tr>
<td>Poor impulse control</td>
<td>0.06</td>
<td>0.35</td>
</tr>
<tr>
<td>Preoccupation</td>
<td>0.47</td>
<td>-0.10</td>
</tr>
<tr>
<td>Expressive immobility</td>
<td>0.75</td>
<td>0.42</td>
</tr>
<tr>
<td>Psychomotor retardation</td>
<td>0.47</td>
<td>0.00</td>
</tr>
<tr>
<td>Positive syndrome with</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Familial affective disorder</td>
<td>-0.49</td>
<td>-0.18</td>
</tr>
<tr>
<td>Familial sociopathy</td>
<td>0.29</td>
<td>0.40</td>
</tr>
<tr>
<td>Years of education</td>
<td>-0.25</td>
<td>0.33</td>
</tr>
<tr>
<td>Marital status</td>
<td>0.06</td>
<td>0.27</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>-0.33</td>
<td>-0.23</td>
</tr>
<tr>
<td>Guilt feelings</td>
<td>0.13</td>
<td>-0.29</td>
</tr>
<tr>
<td>Tension</td>
<td>0.06</td>
<td>0.46</td>
</tr>
<tr>
<td>Uncooperativeness</td>
<td>-0.20</td>
<td>0.48</td>
</tr>
<tr>
<td>Poor attention</td>
<td>0.09</td>
<td>0.42</td>
</tr>
<tr>
<td>Disturbance of volition</td>
<td>0.00</td>
<td>0.18</td>
</tr>
<tr>
<td>Inappropriate affect</td>
<td>0.19</td>
<td>0.53</td>
</tr>
<tr>
<td>Severity of Illness</td>
<td>0.39</td>
<td>0.73</td>
</tr>
</tbody>
</table>

Note.—LTC = Long-term chronic.

1Extracting the shared variance with extrapyramidal symptoms.
2p < 0.05.
3p < 0.02.
4p < 0.01.
5p < 0.001.

Source.—Based on Kay et al. (1986a).

clinical indicators of good prognosis—that is, absence of familial psychosis and presence of various atypical and catatonic phenomena, such as expressive immobility, motor retardation, disorientation, and mannerisms and posturing. Quite the reverse profile—one that connotes poor prognosis—was found for a positive syndrome in the acute stage and, likewise, for a negative syndrome in the chronic stage. Patients of these kinds had a family history of either less affective disorder or more psychosis. They also had poorer premorbid functioning, as suggested by lesser education and failure to marry. Although the interpretation of any particular correlation coefficient must be tempered due to the multiple analyses conducted, the overall differences in pattern far exceeded chance level. In summary, negative and positive symptoms were found to be equally pronounced across decades of illness, and yet their import seemed to differ systematically in correspondence with the evolving illness.

The results on the negative syndrome in chronic schizophrenia were consistent with our previous typological (Opler et al. 1984) and dimen-
Is the Positive-Negative Distinction Valid?

Across the various research perspectives that we pursued, therefore, the results supported the distinctiveness of positive and negative syndromes in terms of basic premorbid, developmental, family history, and prognostic variables. A number of investigators have also provided evidence of psychopharmacological validation, generally reporting less responsiveness of the negative syndrome to neuroleptics (e.g., Meltzer et al. 1986; Breier et al. 1987; Johnstone et al. 1987). Most observations, however, dispel the notion of categorical nonresponse of negative symptoms to neuroleptics. From four separate drug studies, we found additional support for the positive-negative distinction: the positive syndrome alone was exacerbated by anticholinergic antiparkinsonian drugs (Singh et al. 1987) and improved by adjuvant low-dose bromocriptine treatment (Marangell et al. 1989), whereas the negative syndrome alone responded favorably to L-dopa (Kay and Opler 1985–86) and to pimozide (Feinberg et al. 1988). The latter findings suggest that the negative syndrome may be successfully treated and may even be targeted by particular psychopharmacological strategies, including neuroleptics. For the sake of brevity, these investigations will not be elaborated on here, but the details are available in the above-cited publications and in a previous review article (Kay and Opler 1987).

Despite the convergent sources of validation, however, our findings were not congenial with Crow's (1980a, 1980b) hypothesis on the negative syndrome because the data challenge the very premises of the negative syndrome's stability, tendency to worsen over time, neuroleptic nonresponse, and poor prognosis. In fact, given its apparent stage specificity, there seems to be little basis for regarding the negative (or positive) syndrome as a monolithic construct. Only in the chronic negative condition did it appear that a negative presentation may reflect an intransient, residual deficit picture. In early schizophrenia, a negative syndrome was just as prominent but transient, residual deficit picture. In the acute phase. Such a view would regard the negative syndrome as much more benign family history.

One could reasonably argue from the foregoing that the type of negative syndrome that signifies a stable deficit state, as per Carpenter et al. (1988), arises only in the chronic phase. Such a view would regard the chronic negative profile as the marker of an enduring and pernicious form of schizophrenia. Alternatively, it remains possible that the chronic negative picture is simply the visible symptom residue in treatment nonresponders. A related possibility is that we are witnessing an iatrogenic endstate rather than a genuine deficit. To tease apart these explanations clearly requires a prospective, drug-free design with long-term longitudinal followup. Such methodological controls are necessary to guard against contamination by neuroleptic effects that can be expected to alter the nature and course of the illness.

Prospective Drug-Free Assessment

With this aim, we pooled data from four earlier inpatient psychopharmacological studies (Singh and Smith 1973; Singh and Kay 1975a, 1975b, 1976b). The combined sample included 62 schizophrenic patients who were generally young (mean age — 25.2 years), in the subacute phase (mean age — 2.9 years since first hospital admission), and balanced in gender, ethnic composition, and diagnostic subtype. Combined analysis was possible because all four studies used comparable assessments, similar populations, and a within-subjects research design whereby patients served as their own controls.

The studies consisted of a 1- to 2-week drug washout, followed by 2–3 weeks on a drug-free placebo baseline. Patients then received, in double-blind fashion, an individually titrated therapeutic dose of either chlorpromazine or haloperidol, averaging 15 mg/day in haloperidol equivalence. This drug phase lasted 14–18 weeks, after which patients were transferred to another unit or, if possible, were discharged to the community. Fifty-four patients (87%) could be followed up for 3 years to determine at what point, if at all, they had to be rehospitalized.

Symptoms were assessed prospectively in the placebo baseline and again after the neuroleptic phase using the BPRS (Overall and Gorham
and the Psychopathology Rating Schedule (Singh and Kay 1975a). Since these scales were the precursors of the PANSS, we were able to calculate positive and negative scores post hoc, applying the same item combinations as for the PANSS. The sum of 32 individual symptoms provided a measure of total psychopathology.

Four outcome criteria were applied: (1) neuroleptic response was gauged as the degree of improvement in total psychopathology from baseline to final neuroleptic week; (2) residual disorder was the total psychopathology score at the final neuroleptic week; (3) functional reconstitution was judged after the neuroleptic phase by the 5-point Therapy Outcome Rating Scale (Singh and Kay 1979), which measures final disposition in terms of how fully the patient is restored to premorbid levels of social and emotional adjustment; and (4) sustained recovery was quantified as the number of months after treatment until hospital readmission, with a range from 0 (never discharged) to 36 (still in the community after 36 months).

These prospective drug-free data were applied to assess the longitudinal stability, independence, and prognostic significance of negative and positive syndromes in schizophrenia (Kay and Singh 1989). First, we examined the short-term stability during the 2-week drug-free baseline (table 5). High correlations from the end of placebo weeks 1 and 2 were found for both the negative (r = 0.78, p < 0.001) and positive (r = 0.83, p < 0.001) syndromes. Paired t tests revealed no significant changes during this brief time.

Next, to examine the longer-range stability, we compared the initial drug-free week with the final neuroleptic week, 3-4 months later. As indicated in table 5, the longitudinal correlations for the two syndromes were still significant despite the longer interval and the neuroleptic intervention. The 35 percent improvement in negative syndrome with neuroleptic treatment was highly significant (p < 0.001), but not as impressive as the gains in positive syndrome (52%) or total psychopathology (46%). The difference between reduction in negative versus positive scores was in the marginal zone (p = 0.06), which tends to support the relative, but not the absolute, nonresponsiveness of the negative syndrome to these medications.

To assess the independence or relatedness of the syndromes, we performed intercorrelations during both the drug-free and final neuroleptic week. The finding of note was that negative and positive scores were initially unrelated (r = 0.06) but were strongly intercorrelated after neuroleptic stabilization (r = 0.52, p < 0.001), perhaps reflecting the shared benefits from pharmacotherapy. Other analyses during the drug-free state revealed, once again, that chronicity of illness (years since first

Table 5. Stability and changes in syndromal and total psychopathology scales during drug-free baseline and after 14-18 weeks on neuroleptics

<table>
<thead>
<tr>
<th>Basis for comparison</th>
<th>Negative</th>
<th>Positive</th>
<th>Total (Item mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug-free baseline (n = 27)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 1 mean ± SD</td>
<td>20.9 ± 10.85</td>
<td>17.7 ± 6.01</td>
<td>2.05 ± 0.61</td>
</tr>
<tr>
<td>Week 2 mean ± SD</td>
<td>21.3 ± 9.35</td>
<td>16.7 ± 6.88</td>
<td>2.06 ± 0.52</td>
</tr>
<tr>
<td>Change: mean/percent</td>
<td>0.4/1.9</td>
<td>−1.0/−5.6</td>
<td>0.01/+0.5</td>
</tr>
<tr>
<td>Significance: paired t (p)</td>
<td>0.34 NS</td>
<td>0.70 NS</td>
<td>0.32 NS</td>
</tr>
<tr>
<td>Correlation: Pearson r (p)</td>
<td>0.78 (&lt; 0.001)</td>
<td>0.83 (&lt; 0.001)</td>
<td>0.72 (&lt; 0.001)</td>
</tr>
<tr>
<td>Drug-free vs. final neuroleptic week (n = 62)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 1 mean ± SD</td>
<td>22.6 ± 8.97</td>
<td>20.0 ± 6.86</td>
<td>2.36 ± 0.74</td>
</tr>
<tr>
<td>Final week mean ± SD</td>
<td>14.7 ± 7.82</td>
<td>9.7 ± 7.22</td>
<td>1.28 ± 0.78</td>
</tr>
<tr>
<td>Change: mean/percent</td>
<td>−7.9/−35.0</td>
<td>−10.3/−51.5</td>
<td>−1.08/−45.8</td>
</tr>
<tr>
<td>Significance: paired t (p)</td>
<td>6.85 (&lt; 0.001)</td>
<td>10.34 (&lt; 0.001)</td>
<td>9.34 (&lt; 0.001)</td>
</tr>
<tr>
<td>Correlation: Pearson r (p)</td>
<td>0.43 (&lt; 0.001)</td>
<td>0.37 (&lt; 0.005)</td>
<td>0.27 (&lt; 0.05)</td>
</tr>
</tbody>
</table>

Source.—Based on Kay and Singh (1989).
hospital admission) was not associated with negative ($r = 0.13$) or positive ($r = 0.08$) syndrome.

Finally, we analyzed the drug-free baseline data in relation to the four separate outcome criteria to study short-term and longer-range prognosis (table 6). We found first that higher drug-free negative and positive syndromes both predicted a better short-term outcome, as measured by reduction in total psychopathology after 3–4 months of neuroleptic treatment. This observation could simply reflect the principle of "regression to the mean," whereby those patients with a severer initial illness have the greater opportunity for improvement. In keeping with this argument, we also found that higher scores on both syndromes were associated with a greater degree of remaining symptoms after treatment, indicating poorer outcome.

On the other hand, the two syndromes differed clearly with regard to functional reconstitution and sustained recovery. These results were consistent with our other prognostic studies on acute schizophrenia (Kay et al. 1986a; Lindenmayer et al. 1986; Kay and Lindenmayer 1987) but ran counter to prevailing expectations on the positive-negative distinction. As shown in table 6, we found that the drug-free positive syndrome predicted significantly poorer outcome, as judged by more substantial and longer-range criteria. It alone correlated with less complete functional reconstitution after neuroleptic treatment and also with an earlier relapse across the 3-year followup. Severity of total psychopathology yielded a similar prognostic pattern as the positive syndrome.

These findings suggest that a positive syndrome may seem to convey a better outlook because it responds more fully to classical neuroleptics. Over the long course, however, we found it to bear a worse prognosis for both subacute (Kay and Singh 1989) and chronic schizophrenic patients (Kay and Murrill 1990).

Is the Positive-Negative Distinction Sufficient?

Although the foregoing studies uniformly supported the validity of the positive-negative distinction, this does not imply its sufficiency: other factors may still be needed to explain the heterogeneity of schizophrenia. Furthermore, the literature to date has not empirically addressed the relationship of this model to Kraepelin's subtypology for schizophrenia, which still dominates the American diagnostic system (i.e., Research Diagnostic Criteria [Spitzer et al. 1978] and DSM-III-R [American Psychiatric Association 1987]) despite its limited usefulness for treatment and prognostic decisions.

To undertake a fuller study of symptom profiles, we conducted a principal component analysis of the 30 PANSS symptoms in 240 schizophrenic inpatients (Kay 1989b). The results from orthogonal equimax rotation indicated seven factors with eigenvalues greater than 1 that could account for 65 percent of the total variance. Of these, only the first four factors—negative, positive, depressed, and excited—had eigenvalues above 2, embraced a substantial set of symptoms (five or more), and showed factor-specific loadings. Thus, the analysis confirmed the presence of statistically unrelated negative and positive syndromes (factors 1 and 2, respectively) that

<p>| Table 6. Prognostic significance (Pearson r) of drug-free negative and positive syndromes in acute schizophrenia |
|--------------------------------------------------|---------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th><strong>Outcome criteria</strong></th>
<th><strong>Observation period</strong></th>
<th><strong>n</strong></th>
<th><strong>Negative syndrome</strong></th>
<th><strong>Positive syndrome</strong></th>
<th><strong>Total psychopathology</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroleptic response</td>
<td>3–4 months</td>
<td>62</td>
<td>0.28$^1$</td>
<td>0.25$^1$</td>
<td>0.55$^4$</td>
</tr>
<tr>
<td>Residual disorder</td>
<td>3–4 months</td>
<td>62</td>
<td>0.26$^1$</td>
<td>0.28$^1$</td>
<td>0.27$^1$</td>
</tr>
<tr>
<td>Functional reconstitution</td>
<td>3–4 months</td>
<td>62</td>
<td>$-0.14$</td>
<td>$-0.32^2$</td>
<td>$-0.28^1$</td>
</tr>
<tr>
<td>Months to relapse</td>
<td>36 months</td>
<td>54</td>
<td>$-0.08$</td>
<td>$-0.37^3$</td>
<td>$-0.35^3$</td>
</tr>
</tbody>
</table>

$^1p < 0.05.$
$^2p < 0.02.$
$^3p < 0.01.$
$^4p < 0.005.$

Source.—Based on Kay and Singh (1989).
Figure 1. Schematic representation of a pyramidal model of schizophrenia, based on the interrelationship of symptoms from principal component analysis.

Constituent symptoms are as follows:

Individual syndromes:
- **Positive**
  1. Delusions
  2. Grandiosity
  3. Unusual thought content
- **Negative**
  4. Emotional withdrawal
  5. Passive/apathetic social withdrawal
  6. Blunted affect
  7. Poor rapport
  8. Lack of spontaneity and flow of conversation
  9. Poor attention
- **Depressive**
  10. Depression
  11. Guilt feelings
- **Excited**
  12. Excitement
  13. Poor impulse control
  14. Hostility

**Note:** Syndromes appear at the base angles and center, and diagnostic subtypes at the arrow points; polarized dimensions are depicted by the transverse arrows. (Based on Kay and Sevy 1990.)

Syndromes subsumed the main share of variance (36.1%), thereby supporting the factorial validity of the positive-negative distinction. But this two-factor model was, by itself, insufficient to accommodate the phenomenology of schizophrenia.

Plotting the interrelationships among the four factors along X and Y axes, we found that positive, negative, and depressive symptoms clustered separately at divergent foci of the graph. As depicted in figure 1, these factors formed the three angles of a right triangle, with X:Y coordinates of approximately 0:0.9 (positive syndrome), 0.8:0 (negative syndrome), and 0:−0.1 (depressive syndrome). At one corner, a positive syndrome vertex comprised symptoms of grandiosity, delusions, and unusual thought content; at the second corner, a negative syndrome vertex included emotional withdrawal, blunted affect, passive/apathetic social withdrawal, poor rapport, lack of spontaneity and flow of conversation, and poor attention; and at the third corner, a depressive syndrome vertex consisted of depression and guilt feelings. Within this triangular formation, all other psychopathology symptoms could be located. The excitement/impulsivity factor, which included excitement, hostility, and poor impulse control, constituted a fourth pole that yielded a pyramidal model for describing the interrelationship of syndromes in schizophrenia (figure 1) (Kay 1989b; Kay and Sevy 1990).

Intriguingly, the classical symptoms of the Kraepelinian diagnostic subtypes were located at the points of intersection between paired syndromes, as illustrated in figure 1. Thus, the co-occurring syndromes in this model could account for the three subtypes recognized in schizophrenia, as follows: positive-negative...
syndromes—disorganized subtype (e.g., conceptual disorganization, stereotyped thinking); positive-depressive syndromes—paranoid subtype (e.g., ideas of suspicion and persecution, somatic delusions); negative-depressive syndromes—catatonic subtype (e.g., motor retardation, uncooperativeness/negativism). This would suggest that the Kraepelian schizophrenic typology is not phenomenologically "pure": it reflects not single pathological processes but a hybrid of unrelated, co-occurring syndromes that more fundamentally characterize a patient's psychopathology.

Finally, the transverse correspondence between the base vertices and opposing sides in this model (denoted by the broken arrows in figure 1) suggested bipolar dimensions of schizophrenia. Of particular interest, this analysis disclosed a polarized "depression-thought disturbance" axis, which appears to occupy opposite ends of a continuum. The observation is consistent with our follow-up study of chronic schizophrenic patients (see section on "Longitudinal Course of the Syndromes"), from which we discerned that depression and thought disturbance carry contrasting prognostic import (favorable-unfavorable).

The results of our principal component analysis have been recently cross-validated on an independent sample by Lepine et al. (1989) in Paris. Upon applying the French PANSS to 101 patients with a DSM-III-R diagnosis of schizophrenia, they reported that the same four factors emerged from orthogonal varimax rotation, explaining 52.8 percent of the variance. Their study, as ours, found that depression was a significant independent component of schizophrenia, that excitement was a factor distinct from the positive cluster, and that thought disorganization was also divorced from the positive syndrome. The only major difference between the American and French findings was that the positive component emerged as factor 2 in our sample but as factor 4 in theirs.

**Conclusions**

The results and implications of our work may be summarized as follows.

1. Positive and negative syndromes can be reliably and validly assessed.
2. Positive and negative syndromes tend to be normally distributed and statistically independent—that is, not coexclusive; therefore, they are better viewed dimensionally rather than typologically.
3. A purer assessment of these syndromes requires controls for a general degree of illness and neuroleptic status. It has been observed that both positive and negative symptoms are associated with greater severity of overall psychopathology (Kay et al. 1986c; Breier et al. 1987). This, in fact, mediates an intercorrelation between syndromes, which is absent when severity of illness is partitioned out statistically (Kay and Opler 1987). We also found a significant correlation between syndromes when patients were stabilized on neuroleptics but no correlation in the drug-free state. This supports the position advanced by several investigators (e.g., Crow 1980a; Lewine et al. 1983; Pogue-Geile and Harrow 1984; Rosen et al. 1984) that positive and negative syndromes are theoretically independent; that is, they are separate constructs even though in practice they often occur together.

4. In keeping with the literature, we found that the syndromes differ on a broad range of external covariates that may reflect on pathogenesis, such as premorbid functions (cf. Pogue-Geile and Harrow 1984, 1985), family history of psychiatric illness (cf. Dworkin and Lenzenweger 1984), and cognitive profile (cf. Andreasen and Olsen 1982; Liddle 1987a). In chronic schizophrenia, the negative syndrome is uniquely associated with familial psychosis and an ominous cognitive disorder characterized by apparent developmental failure, prefrontal signs, and specific information-processing deficits. From the standpoint of the contribution of nature versus nurture, a combination of genetic and developmental liabilities therefore seems to underlie the negative presentation in schizophrenia.

5. In acute schizophrenia, however, a negative syndrome instead denotes a more benign family history and course of illness. Thus, the meaning of the positive-negative distinction may be considered phase specific, one that varies with the evolving nature of the disease process.

6. The two syndromes are highly stable for the short term in the drug-free state. They also tend to be stable across 3–4 months of neuroleptic intervention despite marked clinical improvements. Stability across a far longer interval, such as 2 years, seems uncertain in the early course of schizophrenia.

7. In response to neuroleptics, both syndromes are significantly improved from baseline even though the reduction in negative symptoms...
is marginally less. These observations are consistent with other recent reports on the neuroleptic effect for negative and positive dimensions of schizophrenia (Meltzer et al. 1986; Breier et al. 1987; Johnstone et al. 1987), which conclude that neither group of symptoms is entirely irreversible. While such findings are compatible with the premise that a positive syndrome represents neurochemical abnormality—that is, dopamine excess—they challenge the more pessimistic view of the negative syndrome.

8. In both our cross-sectional and longitudinal studies, we found no association between chronicity of illness and syndrome scores. Comparably high negative and positive ratings were observed at all phases of the illness, from the acute to the chronic and long-term chronic. The results challenge the assumption that positive symptoms prevail in early schizophrenia while negative symptoms increasingly dominate as the illness advances.

9. Our prognostic analyses also challenge the belief that a negative syndrome bodes poor outcome. In early schizophrenia, a negative presentation actually presaged a favorable course. Our prospective drug-free analyses on mostly subacute schizophrenic patients, as well as our followup of a chronic population, found that a worse long-range outcome was anticipated by a higher baseline positive syndrome. For the short term, however, more severe psychopathology of either description predicted greater symptom reduction with neuroleptics but also greater remaining illness. Accordingly, these data suggest that the prognostic import of the syndromes may vary according to the phase of illness, length of followup, and particular outcome criteria.

10. Notwithstanding the validity and importance of positive and negative syndromes, these are insufficient to accommodate fully the phenomenology of schizophrenia. Based on a principal component analysis of 30 symptoms in 240 patients, we arrived at a 4-point pyramidal model that comprises statistically unrelated negative, positive, depressive, and excited syndromes, which, in their combination, may account for the Kraepelian subtypes and a prognostic dimension of schizophrenia. The findings argue against equating Kraepelin’s subtypes with pure syndromes, since these did not emerge as distinct components; it similarly argues against equating the positive and negative factors with subtypes, since these were not inversely related or coexclusive.

Many of our observations are quite contrary to those reported on the basis of Andreassen’s scales, Krawiecka’s method, and the BPRS. The differences may be a consequence of our using an instrument that is more rigorous or, perhaps, that simply applies different definitions of the constructs. Moreover, our research designs included long-range prospective followup, which may provide a different perspective. A third possible source of variance is in the sampling: we sought to minimize heterogeneity by organizing patients according to chronicity of illness, which indeed proved to be a significant modifier. Finally, in considering the generality of our findings, it should be emphasized that our studies were based on a hospitalized population rather than on one maintained in the community, for which the symptom profile is likely to differ.

Future research will need to address the question of how the various syndromes that are discernible in schizophrenia originate and interact with other fundamental parameters, such as biological markers and course-related measures. Clearly, research is still in its infancy, and progress depends on achieving a more encompassing and integrated model of schizophrenia. At this point, however, phenomenological assessment seems to offer the practicing clinician a means of identifying systematic and valid distinctions within this multifarious condition. The ultimate hope is that a better understanding of the complex presentation will lead to more rational, individually tailored treatments for schizophrenia.

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**Acknowledgments**


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