Positive and Negative Symptoms in Schizophrenia

A Cluster-Analytic Approach

RANDALL L. MORRISON, Ph.D.; ALAN S. BELLACK, Ph.D.; JOHN T. WIXTED, Ph.D.; AND KIM T. MUESER, Ph.D.

The relationships between positive and negative symptoms of schizophrenia and between negative symptoms and social dysfunction were investigated using cluster analysis. Clustering across schizophrenic subjects produced three distinct groups, each characterized by some mix of positive and negative symptoms. Clustering across symptoms and behavioral variables produced a cluster comprising negative symptoms and measures of social adjustment and an additional cluster comprising only measures of social skill. A series of correlations revealed a positive relationship between positive and negative symptom measures. $\chi^2$ analysis revealed a significant relationship between the cluster solution across subjects and classification of patients according to negative symptoms based on previously published criteria. Results are discussed in terms of the implications for the further development and refinement of subclassification schemes for schizophrenia.

Numerous cross-sectional subdivisions for schizophrenia have been proposed, including paranoid vs. nonparanoid (Tsuang and Winokur, 1974), process vs. reactive (Stephens et al., 1966), and good vs. poor prognosis (Vaillant, 1964). Recently, emphasis has been placed on subcategorization based on predominant of positive or negative symptoms (Andreasen and Olsen, 1982). However, negative symptoms are controversial; there is disagreement about their persistence (Lindenmayer et al., 1986; Pogue-Geile and Harrow, 1985) and response to medication (Goldberg, 1985; Johnstone et al., 1978). An even more basic disagreement involves the relationship between positive and negative symptoms. Crow (1980, 1985) hypothesized that positive and negative symptoms represent independent dimensions, and described two distinct schizophrenic syndromes. Type I schizophrenia involves primarily positive symptoms, with an acute and reversible course, good response to neuroleptics, minimal intellectual impairment, and increased dopamine receptors. Type II is characterized by negative symptoms, deteriorating course, poor response to neuroleptics, intellectual impairment, and structural brain changes. According to Crow, the two syndromes can occur simultaneously in the same patient. Alternatively, some patients will only exhibit type I symptoms, while others will only exhibit type II symptoms. A different viewpoint was provided by Andreasen (1982, 1985), who considers positive and negative symptoms to represent continuous variables, which, over a broad spectrum of patients, should be inversely related.

The relationship between positive and negative symptoms has obvious implications for subtyping schizophrenia. Andreasen and Olsen (1982) reported diagnostic criteria to subdivide patients based on current symptoms into positive, negative, and mixed schizophrenia. Applying the criteria to a sample of relatively young, acutely ill schizophrenics, these investigators obtained a negative correlation between positive and negative symptom sets and a roughly equivalent number of patients within each subtype. However, based on a similar sample, Breier et al. (1987) reported that positive and negative symptoms were positively correlated at a pretreatment drug-free condition and after 4 weeks of neuroleptic treatment. Moreover, only two of 19 patients (11%) exhibited a predominantly negative symptom profile while drug-free. This was in contrast to a combined high negative and high positive symptom profile (53%). Other findings have similarly suggested that positive and negative symptoms are not inversely related (Kay et al., 1987; Lewine et al., 1983; Pogue-Geile and Harrow, 1984; Rosen et al., 1984).

Given these contradictions, further study of the cross-sectional relationship between these symptoms is of interest. An alternative to hypothesis-driven subclassification is the use of multivariate analysis/classification strategies to empirically evaluate the relationship among heterogeneous symptoms. Everitt et al. (1971) proposed the use of cluster analysis as a more useful approach to taxonomy in psychiatry than other

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1Department of Psychiatry, The Medical College of Pennsylvania at EPPI, 3200 Henry Avenue, Philadelphia, Pennsylvania 19129. Send reprint requests to Dr. Morrison, The American Medical Association, Department of Mental Health, 535 North Dearborn Street, Chicago, IL 60610.

2Department of Psychology, University of California, San Diego. Preparation for this manuscript was supported in part by NIMH Grant MH36586.
multivariate techniques such as factor analysis, because clustering derives groups with signs and symptoms in common, whereas factor analysis produces groupings of variables. Several investigators have used cluster analysis with schizophrenics (Bartko et al., 1981; Farmer et al., 1983; Strauss et al., 1973), but none included specific negative symptom measures. The present study was designed to consider empirically the cross-sectional relationship between positive and negative symptoms among a cohort of schizophrenics diagnosed according to DSM-III criteria. Cluster analysis was performed on patients’ scores on a variety of psychiatric and social functioning scales with established reliability and validity. It was hoped that empirical categorization would provide information regarding the heuristic utility of subclassification of schizophrenics based on negative symptomatology.

A second major issue is whether social dysfunction should be considered part of the negative symptom construct. In an early discussion, Strauss et al. (1974) distinguished among positive symptoms, negative symptoms, and “disorders in relating.” While Andreasen (1982) incorporated aspects of Strauss et al.’s disorders in relating category into her definition of negative symptoms, Crow (1980) rejected the notion that impaired social competence is a direct reflection of the schizophrenic disease process. Again, objective consideration of the relationship between social dysfunction and negative symptoms is preferable to subjective determinations. Cluster analysis techniques could prove useful in addressing this issue as well.

Thus, this article is intended to examine the relationship between positive and negative symptoms and the relationship of social dysfunction to negative symptoms, using cluster analysis. This report is part of a larger investigation in which measures of psychiatric and social functioning were administered to schizophrenic, schizoaffective, and major affective disorder patients and to nonpatients. The resulting clusters of schizophrenic patients were compared with control subjects on this battery. Also, in order to address the validity of the clusters and to evaluate the relationship between symptoms further, correlational analyses were conducted between measures of positive symptoms, social functioning, and negative symptoms within the schizophrenic sample.

Methods

Subjects were 58 schizophrenic patients, 33 patients with major affective disorder (MAD), and 20 nonpatients. Patients were selected from inpatient psychiatric admissions to the hospital of the Medical College of Pennsylvania at EPPI and were considered for recruitment if they were between 18 and 50 and had no obvious evidence of organic brain syndrome, mental retardation, or alcohol or drug abuse. Patients were interviewed within several weeks of admission with the Schedule for Affective Disorders and Schizophrenia (Spitzer and Endicott, 1978) or the Structured Clinical Interview for DSM-III (Spitzer and Williams, 1985) by a trained psychologist, psychiatrist, or psychiatric nurse. Based on the interview and on hospital records, a consensus diagnosis was reached by the interviewer and one of the first two authors in accordance with DSM-III criteria. Approximately 20% of the interviews were independently reviewed by a second interviewer to evaluate reliability of diagnosis. There was 100% agreement on primary DSM-III diagnosis for this reliability sample. All affective disorder patients had at least a 6-month history of illness. Nonpatients were recruited from the nonprofessional staff and surrounding community of the hospital. They were excluded from participation if they had a history of treatment for a psychiatric disorder. Groups were matched as carefully as possible on age, socioeconomic status (SES; Hollingshead and Redlich, 1958), race, and gender. $\chi^2$ (on gender and race) and an analysis of variance (ANOVA; on age) were nonsignificant. However, as most nonpatients were employed, there was a significant difference between them and patient groups on SES ($F = 34.17; df = 2.108; p < .001$). Also, affective disorder patients had a greater education level than schizophrenics ($F = 3.29; df = 2.108; p < .05$). All subjects were paid for their participation.

A summary of the groups is provided in Table 1. All patients were on medication; mean neuroleptic dose in chlorpromazine equivalents for schizophrenics was $847.61 \pm 483.93$. Overall, both patient samples were young, acute groups, with few prior hospitalizations.

Measures

Interview ratings. The diagnostic interviewer completed the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962), the Maine Scale of Paranoid and Nonparanoid Schizophrenia (MAINE; Magaro et al., 1981) the Raskin Eligibility Depression Scale (RASKIN; Raskin et al., 1967, 1969) and the Global Assessment Scale (GAS; Spitzer et al., 1974). Subjects participated in a second structured interview with an interviewer who was blind to diagnosis. That interviewer rated the subject on the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1982; Andreasen and Olsen, 1982), and two measures of social functioning/adjustment: the Social Adjustment Scale II (SAS; Weissman and Bothwell, 1976; Weissman and Paykel, 1974), and the Quality of Life Scale (QLS; Heinrichs et al., 1984). The SAS yields scores on five dimensions: work adjustment (Work), including adjustment as a student or homemaker;
TABLE 1

Demographic Information

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Gender</th>
<th>Education</th>
<th>SES</th>
<th>Duration of Illness (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenic</td>
<td>31.9 ± 10.29*</td>
<td>34</td>
<td>24</td>
<td>11.9 ± 2.38</td>
<td>4.7 ± .63</td>
</tr>
<tr>
<td>Affective disorder</td>
<td>34.8 ± 10.13</td>
<td>18</td>
<td>15</td>
<td>13.1 ± 2.00</td>
<td>4.1 ± .78</td>
</tr>
<tr>
<td>Nonpatient</td>
<td>32.9 ± 10.18</td>
<td>7</td>
<td>13</td>
<td>12.8 ± 2.37</td>
<td>3.0 ± 1.12</td>
</tr>
</tbody>
</table>

*X ± SD.

household adjustment (House), concerning relationships with household members; external family adjustment (Family), or relationships with relatives outside of the household; social and leisure adjustment (Social); and General Adjustment (General), which is an overall measure. The QLS comprises four dimensions: interpersonal relations (Inter), the capacity to form relationships as well as the extent of social interactions; instrumental role functioning (Role), which focuses primarily on occupational, student, or homemaker roles; intrapsychic foundations (Ipsych), which relates to cognitive, affective, and motivational functioning; and common objects and activities (Common), which assesses participation with objects and activities of everyday life (e.g., reading newspapers, shopping, possessing a wallet, keys, watch).

Approximately 25% of all interviews were rated by a second, independent rater. Reliability was satisfactory for each subscale of each measure; intraclass correlation coefficients (ICC) ranged from r = .64 to .93, with the exception of the activation subscale of the BPRS, for which there was little variability among ratings (ICC = .44).

Behavioral observations. Subjects participated in a role play test of social skills (RPT), which was videotaped and retrospectively rated on a number of behavioral components. Subjects enacted 12 social encounters requiring conversation initiation, resistance of unfair treatment, or expression of appreciation to the interpersonal partner (research assistant). RPT enactments were rated on appropriateness of gaze, speech duration, meshing (smoothness of turn taking and conversational pauses), affect, and two verbal content measures (request/compliance and praise/appreciation). Independent ratings were made of overall social skill. Ratings were made by trained research assistants who were blind to subjects’ group status. One third of the videotapes were scored by an independent rater to provide a reliability check. Reliability was high for all categories, with ICCs ranging from .77 to .92. Component scores were summed for each subject across nonverbal behaviors (gaze, length, meshing, and affect) and verbal content categories.

Demographic and case history information. Premorbid adjustment was measured using the abbreviated version of the Phillips Scale (Harris, 1975) and the Strauss-Carpenter Prognostic Scale (Strauss and Carpenter, 1974). Information was obtained by chart review and interviews with the patient and/or significant others.

Procedure

Clinical records of all admissions were reviewed. The experimental procedures were explained to appropriate patients, and, if consent was obtained, a structured diagnostic interview was conducted. Patients participated in the interview measures and RPT on 2 separate days within 1 week of the diagnostic interview. Testing was initiated after the research team and attending physician concurred that acute symptoms had remitted sufficiently for the patient to participate in the research. Nonpatients were similarly scheduled to complete all measures within a 1-week period.

Results

Two analysis strategies were used to examine the relationship among negative symptoms, positive symptoms, and social dysfunction among schizophrenics: a) cluster analysis to identify (empirically) distinct subgroups of subjects; and b) correlational analyses. A cluster analysis across positive symptom, negative symptom, and social functioning variables was used to derive groupings of empirically similar variables.

CLUSTER ANALYSIS—SUBJECTS

Cluster Descriptions

An agglomerative hierarchical cluster analysis based on average linkage within groups (SPSS; Norusis, 1986) was conducted on standardized scores from each subscale of the SANS and BPRS. Because the negative syndrome construct may include social functioning variables, the Social and General subscales of the SAS as well as the overall social skill rating from the RPT were included in the cluster analysis. The Social and General subscales were included because they were the two subscales on which patients exhibited the greatest range of responding and because items on other subscales were frequently scored as not applicable. For example, some patients had no current work
experience immediately preceding the episode. Six subjects were dropped from the analysis due to missing data. Clustering was stopped at three clusters, based on the values of the fusion coefficient derived during the analysis. That is, the difference between the coefficients for the 3 and 2 cluster solutions was almost three times that of the coefficients for the 3 and 4 cluster solutions.

In Table 2 the psychiatric and social symptom parameters in each cluster are described and the degree to which each variable distinguished between the clusters is indicated. (Scores for MAD and nonpatient groups are included for comparison.)

Cluster 1. The first cluster \((N = 15, 29\% of the sample)\) consisted of patients with mixed psychiatric symptoms (positive and negative symptoms). Most psychiatric symptoms were relatively mild in severity in patients in this cluster. The exceptions were on the apathy and asociality subscales of the SANS and the thought disorder rating from the BPRS, on which there were indications of moderate symptom levels. These patients did not show clinically significant elevations on the alogia or attention subscales of the SANS. Social impairment, as measured by the subscales and RPT performance ratings, was relatively mild in this group.

Cluster 2. The second cluster \((N = 18, 35\% of the sample)\) also included patients with mixed positive and negative symptoms, but these symptoms were of generally moderate severity. This group exhibited moderate elevations on all subscales of the SANS. Social maladjustment was in the moderate range, and these patients obtained the poorest ratings of social skill during the RPT.

Cluster 3. The final cluster \((N = 18, 35\% of the sample)\) consisted of patients with moderate to high scores on all SANS subscales in conjunction with high scores on the thought disorder subscale of the BPRS. Social adjustment was poorest in this cluster, and performance during the RPT was poor.

Cluster Differences—Demographic and Premorbid Variables

The clusters were compared on demographic and premorbid variables using multivariate analysis of variance (MANOVA). A MANOVA on education, SES, medication dose (in chlorpromazine equivalents), number of hospitalizations, length of hospitalizations, premorbid sexual and premorbid social adjustment, and the Strauss-Carpenter Prognostic Scales did not reach significance at the \(p < .05\) level. A \(\chi^2\) analysis on sex was also insignificant.

Relationship between Cluster Analysis and DSM-III Nosology and SANS Typology

The mathematical cluster solution was contrasted with the DSM-III diagnoses (including subtype) of patients using a \(\chi^2\) analysis. This analysis failed to reach significance at the \(p < .05\) level.

A second \(\chi^2\) analysis was calculated to consider the relationship between the results of the cluster analysis and subtyping of patients based on the SANS. The SANS categorization scheme as proposed by Andreasen and Olsen (1982) was expanded to further subdivide mixed patients into those who did not meet criteria for either positive or negative syndrome (mixed-low) and those meeting criteria for both syndromes (mixed-high). There was a significant relationship between the classification strategies \((\chi^2 = 27.89, df = 6, p < .0001)\). Cluster 3 included a preponderance of subjects whose symptoms were mixed-high (12 of 18 cluster 3 patients). Clusters 1 and 2 comprised primarily patients whose symptoms met SANS criteria for positive symptoms or mixed-low.
Validity of the Clusters

To evaluate the external validity of the clusters, groups were compared on psychiatric (GAS, MAINE, RASKIN), social adjustment (QLS and SAS-House\textsuperscript{5}), and social skill (RPT component) measures that had not been included in the cluster analysis. Significance tests on external variables (i.e., on variables that were not used to generate the cluster solution) are considered among the better ways to validate a cluster solution (Aldenderfer and Blashfield, 1984). Separate MANOVAs were calculated for each set of measures (i.e., psychiatric, social adjustment, social skill), followed by univariate ANOVAs and Tukey’s post hoc comparisons where appropriate. The MANOVA on the psychiatric symptom measures was significant at the p < .05 level (F = 2.17; df = 8.88; p < .05). Univariate ANOVAs indicated significant differences among clusters on the GAS (F = 929.21; df = 2.46; p < .001), MAINE (paranoid: F = 353.51; df = 2.46; p < .001; nonparanoid: F = 743.68; df = 2.46; p < .001), and RASKIN (F = 366.70; df = 2.46; p < .001). On all three measures, cluster 3 subjects obtained scores indicative of the most severe psychopathology across the three groups, and cluster 1 subjects displayed the least severe psychopathology. The difference between the ratings obtained by cluster 3 and cluster 1 subjects was significant on each measure. On the RASKIN, all clusters scored in the mildly impaired range. The MANOVA on social adjustment scores was significant at the p < .001 level (F = 6.74; df = 10.70; p < .001). There were significant differences among groups on each measure except Common (the specific F-values ranged from 11.74 to 26.12; df = 2.38; p < .001). On each measure, cluster 1 subjects obtained ratings indicating significantly higher levels of social adjustment than cluster 2 and cluster 3 subjects. On the Inter and Ipsych subscales of the QLS and on the SAS HOUSE subscale, scores for cluster 2 subjects were indicative of significantly greater social adjustment than those obtained by subjects in cluster 3. The MANOVA on RPT components revealed a trend toward significance (F = 1.68; df = 12.88; p < .09). On each behavior, cluster 1 subjects displayed the least impairment.

CLUSTER ANALYSIS—VARIABLES

Cluster analysis can also be used to find homogeneous groups of variables. A second cluster analysis was conducted across the psychiatric and social variables in order to examine the relationship between social dysfunction and negative symptom measures. The absolute value of the correlation coefficient was used as a measure of similarity in this analysis. Cluster membership was computed on the basis of the average linkage within groups (SPSS; Norusis, 1986). The analysis was stopped at four clusters. (Again, the values of the fusion coefficient were considered as a guide to where to halt the analysis.)

Cluster 1. Cluster 1 represented negative psychiatric symptoms, as assessed by the SANS, BPRS anergia, and MAINE nonparanoid subscales. The cluster also included social adjustment, as measured by the SAS and QLS.

Cluster 2. Cluster 2 was a positive symptom cluster and comprised the paranoid subscale of the MAINE and the thought disturbance and hostility subscales of the BPRS.

Cluster 3. This was an anxiety/depression cluster, comprising the anxiety/depression subscale of the BPRS and the RASKIN.

Cluster 4. The fourth cluster included the overall social skill and verbal and nonverbal behavior ratings from the RPT.

Examination of an icicle plot of the cluster analysis revealed several interesting patterns involving negative symptom measures. First, the SAS subscales and the QLS Inter and Ipsych subscales began to cluster with the asociality subscale of the SANS before any of the SANS subscales began to cluster with one another. Also, the apathy, blunting, and asociality scales of the SANS were entered into the negative symptom cluster relatively early in the analysis, whereas alogia and attention are not entered until relatively late.

POSITIVE AND NEGATIVE SYMPTOMS—CORRELATIONAL ANALYSIS

A series of correlation coefficients was calculated to evaluate the relationship between positive and negative symptom measures among schizophrenic subjects. Pearson product-moment coefficients initially revealed a number of significant positive correlations between positive and negative symptoms. However, after controlling for overall psychopathology (Kay et al., 1987) by recalculating the correlation coefficients with GAS scores partialled out, there were no significant correlations between positive and negative symptom scores. Also, there were no significant correlations between SANS scores and neuroleptic dose or depression as measured by either the RASKIN or the anxiety/depression subscale of the BPRS.

\textsuperscript{5}The remaining SAS subscales (Work and External Family) were not included in the analyses because of missing data (e.g., extremely few patients had recently held jobs; therefore, most patients were not rated on the Work subscale).

\textsuperscript{6}More detail regarding the icicle plot, including a copy of the plot itself, is available from the first author.
Discussion

Positive and negative symptoms do not appear to be inversely related and may not individually characterize subgroups of schizophrenic patients. This finding is derived from two distinct analysis strategies: a) cluster analysis of patients according to symptoms and b) correlation coefficients between positive and negative symptom measures. The cluster analysis resulted in three distinct patient groups, each characterized by some mix of positive and negative symptoms. Also, there were a number of significant positive correlations between positive and negative symptom measures. The magnitude of these correlations was reduced to nonsignificant levels when common variance stemming from overall psychopathology was partitioned out. However, even the partial correlations were positive. Thus, the data suggest that positive and negative symptoms are not inversely related and may be independent symptom subtypes.

These findings contrast with those of Andreasen and Olsen (1982) but are consistent with the results of several recent investigations that have failed to derive an inverse correlation between positive and negative symptoms (Breier et al., 1987; Pogue-Geile and Harrow, 1984). Based on their findings, Pogue-Geile and Harrow (1984) conclude that “...negative and positive symptoms may be independent phenomena within schizophrenic patients when assessed concurrently during the early post-acute period” (pp. 378-379).

Among older schizophrenic inpatients and patients with a longer history of illness, Kay et al. (1987) found significant positive correlations between positive and negative symptom scales. However, after partitioning out the common association between positive and negative symptoms and general psychopathology, positive and negative symptoms were inversely correlated. As stated, the partial correlation coefficients that we derived were all positive. Our sample is more similar in age and duration of illness to the Pogue-Geile and Harrow (1984) sample than to that of Kay et al. Perhaps negative and positive symptoms are independent during earlier, more acute phases of the illness, but not during later phases and/or in older patients. Longitudinal studies involving samples of varying chronicity should be conducted to further evaluate this issue.

Our data suggest that negative symptoms may not comprise a unitary phenomenon. Although the SANS subscales are highly intercorrelated, a range of negative symptom profiles occurred across patients. Patients can exhibit symptoms from each SANS subscale or only a subset of symptoms. The number of negative symptoms exhibited by patients may have been related to overall symptom severity, with less-impaired patients experiencing fewer symptoms rather than simply receiving lower scores on each. This issue requires further evaluation. In addition, there was a tendency throughout the cluster analysis of variables toward the identification of two distinct subgroups of negative symptoms. Asociality, apathy, and blunting appear to covary together, and attentional deficits and alogia appear to comprise a second cluster of negative symptoms. These relationships are paralleled in the magnitudes of the correlation coefficients among the SANS subscales.

Only 11% of the sample of Breier et al. (1987) exhibited a predominantly negative symptom profile during a pretreatment drug-free state. Following 4 weeks of neuroleptic treatment, the predominantly negative symptom profile was more prevalent (21%). This was in contrast to a combined high negative and high positive symptom profile (53% drug-free, 5% after 4 weeks neuroleptic treatment). Our findings more closely resemble the pretreatment rates reported by Breier et al., possibly suggesting that our results might have differed after longer neuroleptic treatment of the current episode. Breier et al. observed that both positive and negative symptoms were reduced by neuroleptic treatment, and they discussed the dependence of negative and positive symptom classification on neuroleptic treatment. However, they used only an emotional blunting scale and the anergia subscale of the BPRS as negative symptom measures. They did not assess asociality or social withdrawal. Future research should evaluate the response of a broader range of “negative” symptoms and “defect” states to neuroleptic treatment (Carpenter et al., 1988).

All three patient clusters exhibited social deficits. The severity of social impairment tended to parallel the severity of psychiatric symptoms across clusters. However, even the cluster exhibiting the mildest psychiatric symptomatology exhibited significant interpersonal deficits in comparison to nonpatients.

In a cluster analysis of symptoms of chronic schizophrenics, Farmer et al. (1983) derived two clusters. The larger group was characterized by later onset, good premorbid adjustment, and well-organized delusions. The second group had poor premorbid adjustment, early onset, family history of schizophrenia, and symptoms including bizarre behavior, incoherent speech, and blunted affect. Bartko et al. (1981), in their analysis of 600 subjects from the International Pilot Study of Schizophrenia, identified four clusters. “The subgroups shared the characteristics of paranoid and passivity delusions, auditory hallucinations, restricted affect, and social withdrawal” (p. 946). That all clusters identified by Bartko et al. evidenced social withdrawal and a mix of positive and negative symptoms is con-
Cluster analysis revealed a positive association between positive and negative symptoms. Clustering identified subgroups that cut across DSM-III typologies. While the results of the empirical clustering showed some statistical relationship to SANS typologies, the critical dimension along which the clustering procedure was able to differentiate patients may have been overall severity of psychopathology. Clustering across variables revealed a trend toward multidimensionality within negative symptoms, as well as identification of a separate cluster comprising primarily social skills, as separate from a more generalized negative symptom cluster.

References