Symptom-Oriented vs. Syndrome Approaches to Resolving Heterogeneity of Neuropsychological Functioning in Schizophrenia

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Schizophrenia is a heterogeneous disorder. The syndrome and the symptom-oriented approaches are two methods that have been used to examine differences in psychopathological processes across different patients with schizophrenia. The authors indirectly compared these two approaches in their examination of associations between positive symptoms and neuropsychological performance. Positive syndrome and delusion and hallucination severity scores were compared in respective associations to functioning on 12 neuropsychological variables in 73 stable outpatients with schizophrenia. The individual symptoms of the positive syndrome were associated with relatively distinct patterns of neuropsychological performance, suggesting that the symptom-oriented approach was more sensitive.

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to as the positive, negative, and disorganization syndromes. Many but not all studies that have examined the neuropsychological concomitants of these syndromes have found that the negative and disorganization syndromes are related to impairment in relatively diverse sets of neuropsychological abilities, while the positive syndrome is not highly related to neuropsychological deficits (e.g., 7–9 but see 10–12). However, it is important to note that there has been some inconsistency with respect to neuropsychological associates of the positive syndrome. For example, impairment on the Wisconsin Card Sorting Task (WCST), which is regarded as a measure of frontal lobe functioning, has been positively associated with severity of positive syndrome scores in some studies, unrelated in others, and inversely associated in others.

In contrast to the syndrome approach, the symptom-oriented approach involves investigating individual symptoms. Advocates of the symptom-oriented approach have suggested that it is more useful for understanding psychopathology because there is controversy over which symptoms comprise a syndrome. Moreover, the individual symptoms of a syndrome sometimes may differ in their underlying psychopathological processes. There is a growing body of literature that has utilized symptom-oriented approaches in the investigations of neuropsychological impairment in schizophrenia. However, we are aware of only one published study that has directly compared the individual symptoms of a syndrome in their patterns of neuropsychological functioning. Bentall, Baker, and Kaney found that patients with hallucinations but no delusions performed worse on a self-monitoring task when compared to patients with delusions but no hallucinations, supporting the notion that there are differences in the neuropsychological processes that underlie delusions and hallucinations.

The purpose of this study was to compare the syndrome and the symptom-oriented approaches in examining associations between positive symptoms and neuropsychological performance. This was accomplished by examining the neuropsychological associations of the positive syndrome and those of the two main individual symptoms that comprise the positive syndrome: delusions and hallucinations. It was our expectation, based on the results of Bentall, Baker, and Kaney, that delusions and hallucinations would be associated with different patterns of neuropsychological functioning. If true, this would suggest that the individual symptoms of the positive syndrome have appreciable differences in their underlying neuropsychological processes. Moreover, this would support the notion that a symptom-oriented approach is more sensitive for examining neuropsychological correlates of pathological behavior in schizophrenia.

METHOD

Subjects
This study was part of a multifaceted research project on cognition and symptoms in schizophrenia. The subject group consisted of 73 stable outpatients who met criteria for Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition (DSM–IV) schizophrenia. Diagnoses were made by a clinical psychologist with diagnostic expertise (N.M. Docherty) and were based on information obtained during a Schedule for Affective Disorders and Schizophrenia–Lifetime Version (SADS–L) interview. Subjects with a primary language other than English who met criteria for current DSM–IV substance abuse or dependence or who presented histories of organic impairment were excluded. Subjects who had Global Assessment of Functioning (GAF) scores below 30 were also eliminated.

The subject group consisted of 45 men and 28 women. Fifty-three of the subjects were Caucasian, and 20 were African American. Subjects ranged in age from 18 to 67 years (mean = 36, SD = 10 years) and had an average education of 12.4, SD = 1.5 years and a mean GAF score of 50, SD = 12. Of the 73 subjects, 18 were being prescribed typical antipsychotic medication; 42 were being prescribed atypical antipsychotic medication; six were being prescribed both; and six were not being prescribed any antipsychotic medications. Twenty-seven of the subjects were being prescribed anticholinergic medications. Medication data were missing for one subject.

Procedure

Symptom Rating Scales. The expanded Brief Psychiatric Rating Scale (BPRS); and the Scale for the Assessment of Positive Symptoms (SAPS); were used to measure patients’ symptoms. How the positive syndrome is defined has varied across studies. For example, disorganization symptoms are included in some positive syndrome definitions but not others. For this reason, two different positive syndrome definitions were used in
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this study. The first, which reflects a broadly defined positive syndrome identified in a recent factor analysis study, \(^3\) was calculated by summing the bizarre behavior, unusual thought content, disorientation, hallucinations, and suspiciousness symptom ratings from the BPRS. The second, a more conservatively defined positive syndrome, was calculated by summing the individual global hallucinations and delusion symptom ratings from the SAPS. A negative syndrome score, also identified by Ventura et al. \(^3\) was used. The score was calculated by summing the blunted affect, motor retardation, emotional withdrawal, and self-neglect symptom ratings from the BPRS. Severity of formal thought disorder was measured using the SAPS global formal thought disorder score. The BPRS was employed because it measures a wide range of psychopathology and is commonly used to measure the schizophrenic syndromes. The SAPS was employed as a measure of individual symptoms because the individual SAPS items tend to measure a more narrowly defined scope of psychopathology than individual BPRS items. Symptom ratings were made by graduate student level researchers who had attained acceptable levels of interrater reliability (e.g., intraclass correlation coefficient [ICC] values for SAPS positive syndrome ratings, ICC = 0.84; SAPS global formal thought disorder ratings, ICC = 0.082).

Neuropsychological Tests. The neuropsychological battery included: the Shipley Institute of Living Scales, \(^3\) as a measure of general cognitive ability based on separate vocabulary and abstract concept formation ability subtests; a computerized Wisconsin Card Sorting Task (WCST CV-2), as a measure of executive functions; the Wechsler Adult Intelligence Scale-Revised (WAIS-R) digit span subtest, \(^3\) which includes measures of verbal immediate memory (digit span forward) and working memory (digit span backward); the WAIS-R similarities subtest, \(^3\) which measures the ability to identify abstract relationships; the FAS Verbal Fluency Test, \(^3\) and a visual Dot Test, \(^3\) which measures nonverbal visuospatial working memory functions. The Shipley estimated intelligence quotient (IQ) scores are in standard score format, \(^3\) while the Shipley vocabulary and abstraction subtest scores are in T-score format. Perseverative and nonperseverative error scores from the WCST are represented by the age-normed T-score equivalents. Digit span total and similarities scores from the WAIS-R are represented by their age-normed scaled score equivalents. These tests were selected for use in the present study because their data were in the preexisting dataset. Due to subject attrition and protocol noncompliance, not all 73 subjects completed each individual test.

Analyses. The analyses were conducted in two parts. First, bivariate correlations were calculated between the BPRS- and SAPS-defined positive syndromes and the 12 neuropsychological variables. Second, bivariate correlations were calculated separately between the SAPS global hallucinations score and the SAPS global delusions score and the 12 neuropsychological variables. These correlations were then compared using a Fisher r-to-z test.

RESULTS

Subject Demographic, Clinical Symptoms, and Neuropsychological Test Performance. Means and standard deviations were computed for the broadly defined positive syndrome (mean = 10.8, SD = 4.8), SAPS narrowly defined positive syndrome (mean = 3.9, SD = 3.1), SAPS global hallucination (mean = 2.0, SD = 2.0), SAPS global delusion (mean = 1.9, SD = 1.6), BPRS negative syndrome (mean = 7.0, SD = 3.6), and SAPS global formal thought disorder (mean = 0.8, SD = 1.0) scores. Means and standards were computed for the vocabulary (N = 73; mean = 41.5, SD = 11.0) and abstraction (N = 73; mean = 45.0, SD = 10.1) subsections from the Shipley scores (full scale estimated IQ N = 73; mean = 86.2, SD = 14.5); the perseverative errors (N = 65; mean = 36.6, SD = 12.8), nonperseverative errors (N = 65; mean = 36.5, SD = 12.6), and total trials to completion (N = 65; mean = 37.1, SD = 40.3) scores from the WCST; the forward (N = 76; mean = 6.6, SD = 2.1) and backward (N = 76; M ± SD = 5.4 ± 2.1) scores from the digit span (total score N = 76; mean = 7.9, SD = 2.6); and the similarities (N = 67; mean = 9.1, SD = 2.5), the FAS verbal fluency (N = 64; mean = 32.6, SD = 12), and Dot Test (N = 50; mean = 8.6, SD = 12.2) scores.

The distributions of the original neuropsychological test scores—that is, scores that were not converted to standard or T-score format—each approached normality, with all skew and kurtosis values less than 1.5. The WCST total trials and Dot Test scores were multiplied by a factor of \(-1\) so that increasing scores for all of the neuropsychological tests would represent better performance. Table 1 contains a correlation matrix of the neuropsychological test scores.
There were no significant differences between men and women or Caucasians and African Americans on the BPRS- or SAPS-defined positive syndromes or the SAPS hallucinations or delusions severity scores. Similarly, age, education, or BPRS negative syndrome scores were significantly correlated with any positive syndrome or symptom severity score. However, SAPS global formal thought disorder severity scores were significantly related to BPRS ($r(73) = 0.26, p<0.05$) and SAPS ($r(73) = 0.31, p<0.01$) defined positive syndromes and SAPS hallucinations ($r(73) = 0.28, p<0.05$) and SAPS delusions ($r(73) = 0.27, p<0.05$) scores. These results suggest that the positive syndromes, hallucinations, or delusions severity scores were not significantly related to the demographic score or to negative syndrome scores.

A one-way analysis of variance (ANOVA), with post-hoc Scheffe tests, was conducted to compare four medication groups: typical antipsychotic, atypical antipsychotic, typical and atypical, and no antipsychotic medication. These four groups were compared on positive syndrome and symptom severity scores and neuropsychological performance scores. There were no significant differences among the groups on BPRS- or SAPS-defined positive syndromes, SAPS hallucinations or delusions, SAPS formal thought disorder, or BPRS negative syndrome severity scores. Likewise, there were no significant group differences regarding neuropsychological performance, although there was a trend among subjects who were being prescribed typical antipsychotic medications to have poorer performance on the Shipley verbal, WAIS-R digit span forward, and similarities tests, compared to subjects being prescribed atypical antipsychotics. Subjects who were prescribed anticholinergic medication performed significantly poorer on WAIS-R digit span forward scores ($t = 2.24, df = 67, p<0.05$), and at a trend level on the digit span total scores, compared to subjects not being prescribed anticholinergic medication. Generally speaking, differences in medications accounted for little difference in symptoms among these stable outpatients and accounted for only a few relatively small differences in neuropsychological performance.

**Positive Syndrome Severity Scores and Neuropsychological Performance.** Bivariate correlations were calculated between the BPRS-defined positive syndrome, the SAPS-defined positive syndrome, and the 12 neuropsychological test scores. These results are presented in Table 2. The BPRS-defined positive syndrome scores were significantly and positively associated with Dot Test scores and inversely associated with similarities test scores at a trend level. Likewise, the SAPS-defined positive syndrome scores were significantly and positively associated with Dot Test scores and inversely associated with similarities test scores. The BPRS-defined positive syndrome and the SAPS-defined positive syndrome scores did not differ in their respective correlations to any of the 12 neuropsychological performance scores. They were not associated with any other measures. These results suggest that severity of both positive syndromes was associated at or above the trend level, with better performance on the visual working memory task and poorer performance on the similarities test. Not surprisingly, the BPRS-defined positive syndrome and SAPS-defined positive syndrome scores were highly correlated with each other ($r = 0.86, df = 73, p<0.001$).

<p>| TABLE 1. Correlation Matrix of Neuropsychological Test Performance Scores |
|------------------------------------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|</p>
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<th>7</th>
<th>8</th>
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<td>3. Abstraction section</td>
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<td>4. WCST–Total trials</td>
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<td>.20</td>
<td>.11</td>
<td>.06</td>
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</table>

Increasing test scores reflect better performance.

**Correlation is significant at the 0.01 level (2-tailed).

*Correlation is significant at the 0.05 level (2-tailed).
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Delusions, Hallucinations, and Neuropsychological Test Performance. Scale for the Assessment of Positive Symptoms hallucination and delusion severity scores were significantly associated with each other (r = 0.57, df = 73, p<0.001). Bivariate correlations were calculated between these symptom severity scores and the 12 neuropsychological performance scores (Table 2). SAPS hallucination scores were significantly and inversely related to Shipley abstraction scores and WCST total trials-to-completion scores and were related to similarities scores at the trend level. SAPS delusion scores were significantly positively associated with digit span backward and dot test scores. These results indicate that severity of hallucinations was associated with worse performance on two tests of abstraction ability, as measured by the similarities and Shipley abstraction tests, and poorer overall performance on the WCST test. Severity of delusions was associated with better performance on the two working memory tasks, the digit span backward, and the visual dot test.

In order to examine whether SAPS defined delusions and hallucinations were associated with different patterns of neuropsychological performance, their respective correlations to the 12 neuropsychological performance scores were compared using the Fisher r-to-z test (Table 2). SAPS delusion and hallucination severity scores differed significantly in their relationships to the Shipley estimated IQ, Shipley vocabulary test, and WCST nonperseverative errors scores, and, at a trend level, in their relationships to the Shipley abstraction scores, WCST total trials, and the visual dot test scores.

In sum, the SAPS defined hallucination and delusion scores differed in their respective associations to six of the 12 neuropsychological performance variables at or above the trend level.

DISCUSSION

Consonant with many previous studies of neuropsychological functioning in schizophrenia, positive syndrome severity scores were significantly associated with functioning on only a few of the neuropsychological tests. Likewise, when hallucination and delusion severity scores were examined separately, they were related to performance on only a few of the 12 neuropsychological variables. However, when hallucination and delusion severity scores were compared in their respective associations to neuropsychological functioning, they differed at or above the trend level on one-half of the neuropsychological variables. There were no substantive effects of demographic, medication type, or negative or disorganization syndrome severity variables in these results, suggesting that delusions and hallucinations are associated with relatively different patterns of neuropsychological functioning and presumably have at least some important differences in their respective underlying neuropsychological processes.

The notion that the symptom-oriented approach, as compared to the syndrome approach, may be a more useful method for investigating how neuropsychological functioning differs across the different manifesta-

TABLE 2. Bivariate Correlations Between the BPRS Positive Syndrome, and SAPS Positive Syndrome, Global Hallucinations (Hall.) and Delusions (Del.) Severity Ratings and Neuropsychological Test Performance Scores, and p Value of Fisher r-to-z Comparison of the SAPS Hallucination vs. Delusions Scores in Their Respective Associations to Neuropsychological Performance

<table>
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<tr>
<th>Neuropsychological Tests</th>
<th>N</th>
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<th>SAPS</th>
<th>Hall.</th>
<th>Del.</th>
<th>p value of Hall. vs. Del.</th>
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<td>.10</td>
<td>.11</td>
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<tr>
<td>WCST–Total trials to completion</td>
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<td>-.17</td>
<td>-.19</td>
<td>-.26*</td>
<td>-.06</td>
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<td>Non-persever. errors, T-score</td>
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<td>-.09</td>
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<td>Digit Span, age corrected scaled score</td>
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<td>.10</td>
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<td>Forwards score</td>
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<td>.18</td>
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<td>.08†</td>
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Increasing test scores reflect better performance.

*Correlation is significant at the 0.05 level (2-tailed).

†Correlation is significant at the 0.10 level (2-tailed).
tions of schizophrenia was supported by two findings from this study. First, severity scores of the two main individual symptoms that comprise the positive syndrome, hallucinations, and delusions showed appreciable differences in their respective neuropsychological associates. Second, the conservatively and liberally defined positive syndromes did not differ much from each other, even though the liberally defined syndrome included ratings of suspiciousness, bizarre behavior, and disorientation symptoms. Thus, the positive syndromes were associated with similar neuropsychological profiles despite significant differences in the neuropsychological correlates of the individual symptoms that constitute these syndromes.

It would be premature, based solely on the results of this study, to attempt to identify specific neuropsychological substrata that differentially underlie hallucinations versus delusions. The general trend was for hallucination severity ratings to be associated with poorer neuropsychological performance and for severity of delusion ratings to be associated with better neuropsychological performance, particularly on tests of working memory. It is surprising that severity of delusions was associated with better performance on any test used in this study. One possible explanation for this is that the patients who presented with more severe delusions tended to be of a paranoid subtype. This would be consistent with evidence suggesting that the cognitive profiles of paranoid patients more closely approximate normality when compared to other patients with schizophrenia. For this to be true, however, paranoid subtype patients in our sample would have had to have lower hallucinations ratings compared to the other patients. With respect to the literature on severity of hallucinations in paranoid patients, there is mixed support for this idea. On one hand, paranoid and hallucinatory symptoms have loaded on different clusters in a factor analysis of items in a symptom ratings scale administered to a group of outpatients with schizophrenia. However, severity of hallucinations has not differed between paranoid subtype patients versus undifferentiated subtype patients in one study, versus hebephrenic patients in another study and have loaded on similar factors in other studies. This study did not include subtype diagnoses for patients, which would be a pertinent analysis in future research.

Several limitations to the study apply. First, it was exploratory in design, and no formal attempt to control for type II errors was included. Second, most of the subjects in the present study were being prescribed psychotropic medication. While there were no apparent substantive effects of medication type on hallucination or delusion severity scores, analyses such as these are not conclusive since medications are not prescribed randomly. Third, although there were a number of significant differences between delusions and hallucinations in their respective neuropsychological associates, it is important to note that the correlations between the individual positive symptoms and the neuropsychological functioning scores were moderately significant at best. However, there appear to be different patterns of associations for the symptoms. Finally, the sample size used was composed of stable, yet relatively chronic outpatients. It is unclear whether the results of this study would generalize to other patient groups.

In summary, this study replicated findings that the positive syndrome has few clinically significant neuropsychological associates. There were no substantive differences between a conservatively versus liberally defined positive syndrome in terms of neuropsychological correlates. However, when analyzed independently, hallucination, and delusion severity scores were associated with different patterns of neuropsychological functioning, suggesting that a symptom-oriented approach to investigating neuropsychological functioning across heterogeneous manifestations of schizophrenia may be more sensitive and informative than the syndrome approach.

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