Language Comprehension in Schizophrenia: Trait or State Indicator?

Ruth Condray, Daniel P. van Kammen, Stuart R. Steinhauer, Annette Kasperek, and Jeffrey K. Yao

Language comprehension, measured by the Luria-Nebraska Relational Concepts Factor Scale, was evaluated twice in 15 male DSM-III-R schizophrenic patients during a controlled double-blind haloperidol maintenance (without anticholinergics) and placebo replacement protocol. Fifteen male normal controls were tested once. Patients and controls were matched on age and education. Language comprehension was significantly reduced in patients under both pharmacologic conditions, as compared with controls. Patients' comprehension accuracy did not differ significantly between neuroleptic-treatment and placebo-replacement conditions. Patients' comprehension accuracy was independent of positive symptoms, anxiety-depression, measures of clinical course, and CSF and plasma monoamines. Comprehension accuracy was also not associated with patients' educational level or WAISR measures of their intellectual and short-term memory functioning. Patients' comprehension performance was significantly associated only with the negative symptom anhedonia-asociality during haloperidol maintenance. Thus, language comprehension in schizophrenic patients was independent of changes in pharmacologic treatment and the positive symptoms of psychosis. Results suggest language comprehension may represent a stable or trait characteristic in schizophrenia.

Key Words: Schizophrenia, language comprehension, neuroleptic-treatment, placebo-replacement

Introduction

Language comprehension involves processing words presented sequentially within a semantic context. This language skill requires the ability to understand logical relationships expressed in grammatical constructions of variable complexity (Luria 1980; Marslen-Wilson 1975). Disturbances in this cognitive capacity have been documented for schizophrenic patients (Faber and Reichstein 1981; Green et al. 1979; Kagler 1983; Morice and McNicol 1985; Thomas and Huff 1971) and for their children (Hallet and Green 1983) and nonpsychotic adult family members (Condray et al. 1992). The presence of this cognitive disturbance in the nonpsychotic relatives of patients suggests that comprehension dysfunction may be associated with familial risk for schizophrenia (i.e., a vulnerability indicator). It is not known, however, whether this language disturbance is stable in patients across changes in clinical state, such as during exacerbations of clinical symptoms or following changes in pharmacologic treatment.

Vulnerability indicators are dysfunctions that are associated with psychiatric disorder and familial risk for psy-
chopathology. These indicators are present in both patients and unaffected family members, and are independent of changes in clinical state (Nuechterlein and Dawson 1984; Nuechterlein et al. 1992; Zubin and Spring 1977; Zubin and Steinhauser 1982). In contrast, episode or state indicators are dysfunctions that appear only during active phases of psychiatric disturbance. A third type of indicator was proposed by Nuechterlein and associates (Nuechterlein and Dawson, 1984; Nuechterlein et al. 1992) to describe behaviors that are abnormal during periods of clinical stability, and increase in severity during periods of clinical exacerbation (i.e., a mediating vulnerability indicator). The presence of abnormal language comprehension in schizophrenic patients and their non-psychotic family members suggests this cognitive dysfunction represents a vulnerability indicator of schizophrenia, but it is not known whether comprehension disturbance becomes more severe during changes in clinical state.

The effects of neuroleptic medication on cognitive performance in schizophrenic patients differ according to the type of cognitive function assessed (for reviews, see Medalia et al. 1988; Saphir and Strauss 1989). The association between pharmacologic treatment and cognitive performance therefore requires specification by type of cognitive function. Medalia et al. (1988) noted in their review that an absence of sufficient data made it impossible to evaluate the effects of neuroleptics on basic language function in schizophrenic patients. Comprehension performance in this patient population has typically been measured during treatment with a variety of pharmacologic agents, including antipsychotic and anticholinergic medications.

Exceptions include studies in which the single evaluation of language function occurred prior to the initiation of neuroleptic treatment (Faber and Reichstein 1981; Saykin et al. 1994). In a recent study, neuropsychological functioning, including a general language factor, was evaluated at admission when patients were drug-free and at follow-up after stabilization on neuroleptic medication (Cannon et al. 1994). We are not aware of studies in which language comprehension performance was evaluated in schizophrenic patients during controlled double-blind medication maintenance and placebo replacement protocols.

Determining whether language comprehension is modulated by pharmacologic agents is highly relevant to our efforts to understand the neuropathology of schizophrenia. Converging evidence suggests an association between cognitive dysfunctions of schizophrenia and reductions in the dopaminergic tone of the prefrontal cortex (for a review, see Cohen and Servan-Schreiber 1992). Moreover, dopaminergic tone may be particularly important when tasks require the processing of contextual information (Cohen and Servan-Schreiber 1992). One implication of those findings is that language comprehension, which requires the processing of contextual information, may be influenced by the balance between monoamine neurotransmitter systems. Therefore, neuroleptic treatment of schizophrenic patients, which may stabilize the relationships between those neurotransmitter systems (Hsiao et al. 1993; Kuhn et al. 1993), may also be associated with improvement in comprehension performance.

The present study addressed the following questions: 1) Is language comprehension stable in schizophrenic patients across neuroleptic-treatment and placebo replacement phases? 2) Is language comprehension in patients associated with clinical stability, as indicated by ratings of clinical symptomatology? As noted, a trait or vulnerability indicator involves performance dysfunction that is independent of clinical state. Language comprehension as a trait characteristic will be suggested by performance that does not differ between neuroleptic treatment and placebo replacement conditions, and that is independent of ratings of clinical symptomatology.

**Method**

Research questions were examined using a repeated measures design in which language comprehension was evaluated in the same schizophrenic patients under two pharmacologic conditions: 1) haloperidol maintenance without anticholinergic medication, and 2) placebo replacement. The primary analysis involved a comparison of patients' language performance between medication conditions. An additional comparison was conducted between the performance of patients and normal controls who were matched on age and education. Normal controls were tested once. The measure of language comprehension was the Luria-Nebraska Relational Concepts Factor Scale, which has been successful in discriminating patients with and without neurological injury (Golden et al. 1985), and in distinguishing the relatives of schizophrenic patients from control subjects in previous studies conducted in our laboratory (Condray and Steinhauser 1992; Condray et al. 1992; Watson 1988). High test-retest reliability has been reported for this scale in psychiatric inpatients (Plaisted and Golden 1982). Additional measures were included to examine associations between patients' language comprehension performance and indicators of their clinical state; ratings of positive (BPRS), negative (SANS), and mood (BPRS) symptoms. Associations between language comprehension performance and CSF and plasma monoamines were explored. The relationship between patients' language comprehension performance and their educational level and general intellectual functioning (WAIS-R), including short-term memory function, was also evaluated.

**Subjects**

Subjects were 15 physically healthy male veterans who were diagnosed with DSM-III-R schizophrenia or schizoa-
Table 1. Demographic Characteristics of Schizophrenic Patients (n = 15) and Normal Controls (n = 15)* Mean ± SD

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>Schizophrenic patients</th>
<th>Normal controls</th>
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<tbody>
<tr>
<td>Age</td>
<td>36.2 ± 8.8</td>
<td>35.2 ± 9.1</td>
</tr>
<tr>
<td>Education (years)</td>
<td>13.4 ± 1.8</td>
<td>14.0 ± 1.9</td>
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</table>

 Effective disorder (American Psychiatric Association 1987), and who were admitted voluntarily to the Schizophrenia Research Unit (SRU) at the Highland Drive VA Medical Center in Pittsburgh, PA. Diagnoses of patients were based on the results of the Structured Clinical Interview for DSM-III-R (SCID: Spitzer et al 1989), which was conducted shortly after admission to the inpatient unit. Exclusion criteria for the language processing protocol were: history of major medical or neurological disorders, current DSM-III-R Substance Use Disorder, reading level less than 8th grade as determined by the Wide Range Achievement Test (WRAT), and WAIS-R Full-scale IQ less than 80.

To provide comparison data for the patient group, language comprehension performance of 15 physically healthy male normal controls is also reported. This normal control group was matched with the patient group on age and education. Normal controls were diagnosed as No Lifetime Psychiatric Disorder. Diagnoses of controls were based on the results of the Structured Clinical Interview for DSM-III-R (SCID: Spitzer et al 1989) or the Schedule for Affective Disorders and Schizophrenia-Lifetime (SADS-L: Spitzer and Endicott 1979). These normal control individuals had previously participated in cognitive and language processing research protocols conducted in the Biometrics Research Laboratory at the Highland Drive VA Medical Center. Language comprehension data for nine of these normal control subjects were reported previously (Conway et al 1992).

**CHARACTERISTICS OF SAMPLE.** Table 1 shows average age and number of years of education for the schizophrenic patients and normal controls evaluated in this study. Age and number of years of education did not differ significantly between the two groups. Table 2 presents clinical and general intellectual characteristics of the schizophrenic patients. General intellectual functioning of this patient group was well within the normal range for the WAIS-R Verbal, Performance, and Full-scale intelligence.

**Procedures.**

Informed consent following explanation of procedures was obtained from patients prior to participation in both the Schizophrenia Research Unit parent protocol and the present language processing protocol. Informed consent following explanation of diagnostic and language processing procedures was obtained for normal controls. Patients were not reimbursed for their participation. Normal controls were paid $50 for completion of the language protocol.

**HALOPERIDOL MAINTENANCE AND PLACEBO REPLACEMENT PARENT PROTOCOL.** Language comprehension was tested in the above described 15 schizophrenic patients following clinical stabilization on haloperidol and during placebo replacement. The mean test-retest interval for this sample of patients was 30.4 days (SD = ± 10.6). Clinical staff and patients were blind to medication status. Patients received a low monoamine, caffeine-restricted, and alcohol-free diet for the duration of this protocol. Patients received active medication or placebo orally in unmarked capsules that were identical in number and appearance. All anticholinergic, sleep, and pain medications were discontinued at least 2 weeks prior to the test week for research procedures during the medication maintenance phase. This occurred after patients had received a stable dose of haloperidol for a minimum of 2 weeks and were rated as clinically stable by the clinical therapist. Placebo replacement immediately followed the test week for research procedures during haloperidol maintenance, and the reverse order occurred for those patients who entered the protocol drug-free (i.e., administration of haloperidol immediately followed the test week for research procedures during the placebo phase). The mean number of days patients received haloperidol prior to testing was 76 ± 64 days (range: 17–210 days) (n = 12 patients). The data for two patients represented extreme values (> 1.5 years on haloperidol), and this information was missing for one patient. The mean number of days patients received placebo prior to testing was 13 ± 4 days (range: 13–26 days) (n = 14 patients). One patient was neuroleptic-naive. For 13 patients, the order of pharmacologic condition was haloperidol maintenance followed by placebo replacement, and the order for the remaining two

Table 2. Clinical Characteristics and General Intellectual Functioning of Schizophrenic Patients (n = 15)

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Mean ± SD</th>
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<tbody>
<tr>
<td>Age at first hospitalization</td>
<td>23.6 ± 5.2</td>
</tr>
<tr>
<td>Duration of illness (years)</td>
<td>13.2 ± 8.9</td>
</tr>
<tr>
<td>Number of psychiatric hospitalizations</td>
<td>7.9 ± 5.7</td>
</tr>
<tr>
<td>Haloperidol dose (mg/day)</td>
<td>9.7 ± 4.4</td>
</tr>
<tr>
<td>DSM-III-R diagnosis (N/Percentage)</td>
<td></td>
</tr>
<tr>
<td>Schizophrenia, paranoid</td>
<td>7 (46.6%)</td>
</tr>
<tr>
<td>Schizophrenia, undifferentiated</td>
<td>4 (26.6%)</td>
</tr>
<tr>
<td>Schizoaffective</td>
<td>4 (26.6%)</td>
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<table>
<thead>
<tr>
<th>General intellectual functioning</th>
<th>Mean ± SD</th>
</tr>
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<tbody>
<tr>
<td>WAIS-R Verbal IQ</td>
<td>95.7 ± 9.9</td>
</tr>
<tr>
<td>WAIS-R Performance IQ</td>
<td>94.9 ± 8.6</td>
</tr>
<tr>
<td>WAIS-R Full Scale IQ</td>
<td>94.4 ± 6.9</td>
</tr>
<tr>
<td>WAIS-R Digit Span</td>
<td>93 ± 2.8</td>
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</table>
patients was placebo replacement followed by haloperidol maintenance (one patient entered drug-free; one patient entered neuroleptic-naïve). Antipsychotic medication was reinstated for patients who met the following criteria for symptom exacerbation ("relapse"): 1) an increase of three or more points on the Bunney-Hamburg scale (Bunney and Hamburg 1963) rated by the nursing staff, with an absolute score of seven or more points over a period of at least three consecutive days; and 2) a concurrent increase on the Bunney-Hamburg scale rated weekly by the clinical therapist.

**LANGUAGE COMPREHENSION AND GENERAL INTELLECTUAL FUNCTIONING.** Language comprehension was evaluated using the Relational Concepts Factor Scale (R2) from the Luria-Nebraska Neuropsychological Battery (Form I) (Golden et al. 1985). Items on this scale successfully discriminated patients with and without neurological injury (Golden et al. 1985), and distinguished relatives of schizophrenic patients from control subjects in our previous family studies (Condray and Steinhauer 1992; Condray et al. 1992; Watson 1988). High test-retest reliability ($r = .85$, $p < .01$) over an interval of 8 months has been demonstrated for this scale in a sample of psychiatric inpatients (Plaisted and Golden 1982, p. 166). The scale is administered orally and includes items that measure the understanding of logical relationships expressed through syntactic connectives (e.g., conjunctions and adverbs), word order (e.g., subject-verb-object), and interclausal relations (independent and dependent clauses). Types of grammatical constructions include comparative, inverted, and complex embedded sentences. Item 132 from this scale is presented as an example (Factor Scale R2: Golden et al. 1985): “The woman who worked at the store came to the school where Mary studied to give her a talk. Tell me, who gave a talk? (Pause for a response). Tell me, what was Mary doing?” The response measure used in the present study was number of errors.

General intellectual function of patients was evaluated using the WAIS-R IQ. This test was administered during the initial diagnostic evaluation and clinical stabilization period, and before the first test procedures week. IQ data were not available for control subjects.

**RATINGS OF CLINICAL SYMPTOMATOLOGY.** Clinical symptoms were rated weekly by the clinical staff of the Schizophrenia Research Unit who were blind to patients’ medication status. Ratings of symptoms reported in this study were based on the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham 1962) and the Schedule for Assessment of Negative Symptoms (SANS; Andreasen 1982). Patients were evaluated by the same clinician under each pharmacologic condition.

**CSF AND PLASMA MONOAMINES.** The cerebrospinal fluid (CSF) and plasma measures reported in the present study are based on samples obtained in the Schizophrenia Research Unit parent protocol during the test weeks for research procedures under each pharmacologic condition. CSF was obtained by lumbar puncture (LP) conducted between 7:30–8:00 AM following fasting and bed rest beginning at 11:00 PM on the preceding evening. Plasma was also drawn while patients were in a fasting state 24 hours prior to the LP procedure.

The method used to determine cerebrospinal fluid (CSF) levels of 3-methoxy-4-hydroxyphenylglycol (MHPG), 5-hydroxyindoleacetic acid (5-HIAA), and homovanillic acid (HVA) was essentially the same as that described by Scheinin and associates (1983). The procedure used for the determination of norepinephrine (NE) from CSF was a modified method of Lin and colleagues (1984). Plasma levels of HVA and MHPG were determined using the method described by Gerhardt and associates (1986).

**Data Analyses**

Research questions were tested using $t$-tests and correlation analyses. The group comparisons of language comprehension performance (patients versus controls) showed unequal group variances; therefore, results of those $t$-tests are based on the separate variance estimates, which are designated as separate $t$. Matched or paired $t$ tests were used to compare patients’ language comprehension performance and the indicators of their clinical state between pharmacologic conditions. Nonparametric tests (Mann-Whitney and Wilcoxon tests) were conducted to verify robustness of parametric analyses. Results were not altered by application of these nonparametric tests. Correlation analyses were conducted to examine relationships between language comprehension and clinical state under each medication condition, as well as between language comprehension under each medication condition and measures of intellectual and short-term memory functioning. Nonparametric correlation (Spearman’s rho) was used for these analyses to correct for extreme scores and ties in the data. To reduce the potential for Type I errors, the standard significance level of $p = .05$ was adjusted for these multiple comparisons using Bonferroni correction for five families of variables (Grove and Andreasen 1982) as follows: 8 clinical symptoms (2 positive, 5 negative, and 1 mood) rated twice = 16 ratings-adjusted $p = .003$; 4 CSF and 2 plasma measures evaluated twice = 12 variables-adjusted $p = .004$; the two evaluations of language comprehension correlated with 3 measures of clinical course = 6 correlations-adjusted $p = .008$; the two evaluations of language comprehension correlated with 4 measures of cognitive functioning (education and IQ) = 8 correlations-adjusted $p = .006$; and the
5 correlations of comprehension performance and aspects of pharmacologic condition—adjusted \( p = .01 \) [2 evaluations of comprehension performance with dose and length of time administered haloperidol = 4 correlations: comprehension during placebo and length of time administered placebo prior to testing = 1 correlation].

Results

Language Comprehension Performance

Table 3 shows the average number of errors on the measure of language comprehension for patients under each medication condition and for the normal control group. The mean number of comprehension errors was significantly greater for the schizophrenic patient group during both medication phases than for the normal control group: normals versus patients during haloperidol maintenance (separate \( t_{10} = 3.32, p = .0043 \)), and normals versus patients during placebo replacement (separate \( t_{10} = 3.90, p = .001 \)). Thus, patients showed significantly reduced comprehension performance during both pharmacologic conditions, as compared with normal controls.

Patients’ comprehension performance did not differ significantly between the haloperidol maintenance and placebo replacement conditions (matched \( t_{11} < 1, p = .71 \)). Although performance across the two test sessions was not significantly associated, examination of magnitude and type of performance changes showed frequencies that approximate a normal distribution. The majority of patients \( (n = 9/15 = 60\%) \) showed either no change at all \( (n = 7) \), or a change of only 1 error \( (n = 2) \). Type of change was distributed similarly: comprehension accuracy across test sessions improved in one-fourth of the group \( (n = 4/15 = 26.6\%) \), decreased in one-fourth of the group \( (n = 4/15 = 26.6\%) \), and did not change in approximately one-half of the group \( (n = 7/15 = 46.6\%) \). Thus, language comprehension performance in this group of schizophrenic patients did not differ significantly as a function of pharmacologic condition; although they did show greater variability across test sessions than was previously observed in psychiatric inpatients (Plaisted and Golden 1982).

Though group differences were highly significant, the proportion of schizophrenic patients who showed abnormal comprehension performance, as defined psychometrically \( (T \geq 60) \), depended on the group used as the standard of comparison. Normative data reported by Golden et al. (1985) were based on standardization studies that included neurologically impaired patients with no evidence of psychiatric disorder and a control group of general medical inpatients without neurological impairment. When \( T \) scores reported by Golden et al. (1985) were used as the standard, the proportion of our patient group who showed abnormal performance was very low \( (2/15 = 13\% \) during haloperidol maintenance; \( 1/15 = 7\% \) during placebo replacement). In contrast, when \( T \) scores were calculated using the performance of our normal control group as the standard of comparison, the proportion of schizophrenic patients who exhibited abnormal performance was very high \( (11/15 = 73\% \) during haloperidol maintenance; \( 12/15 = 80\% \) during placebo replacement).

ASSOCIATION BETWEEN LANGUAGE COMPREHENSION PERFORMANCE AND EDUCATION AND INTELLIGENCE

Level of education was not associated with patients’ comprehension performance during either haloperidol maintenance \( (\rho_{15} = .007, p > .05) \) or placebo replacement \( (\rho_{15} = -.41, p > .05) \). Level of education was also not correlated with language comprehension in normal controls \( (\rho_{15} = .23, p > .05) \). Moreover, patients’ intelligence was not associated with their comprehension performance during either pharmacologic condition \( (WAIS-R Verbal IQ: \rho_{15} = -.14, p > .05; \rho_{15} = -.13, p > .05) \), and \( WAIS-R Full Scale IQ: \rho_{15} = -.18, p > .05; \rho_{15} = -.20, p > .05 \). Patients’ language comprehension was also not associated with short-term memory performance \( (WAIS-R Digit Span: \rho_{15} = -.27, p > .05; \rho_{15} = -.16, p > .05) \).

Indicators of Clinical State

The hypothesis that language comprehension represents a stable characteristic in schizophrenia was further evaluated by examining associations between patients’ comprehension performance and measures of their clinical state; ratings of positive, negative, and mood symptoms, and CSF and plasma monoamines.

Associations between Language Comprehension and Clinical Symptoms. Table 4 presents average ratings of positive (BPRS), negative (SANS), and mood (BPRS) symptoms for patients during the test week under each pharmacologic condition.
Table 4. Mean Ratings of Positive, Negative, and Mood Symptoms in Schizophrenic Patients (n = 15) Evaluated during Haloperidol Maintenance and Placebo Replacement Phases (Mean ± SD)

<table>
<thead>
<tr>
<th>Clinical symptoms</th>
<th>Haloperidol maintenance</th>
<th>Placebo replacement</th>
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<tbody>
<tr>
<td><strong>Positive symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BPRS Thinking Disturbance</td>
<td>4.7 ± 2.5</td>
<td>5.5 ± 3.3</td>
</tr>
<tr>
<td>BPRS Psychosis</td>
<td>10.5 ± 3.0</td>
<td>12.9 ± 5.9</td>
</tr>
<tr>
<td><strong>Negative symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SANS Global Affective Flattening</td>
<td>2.3 ± 0.9</td>
<td>2.3 ± 1.1</td>
</tr>
<tr>
<td>SANS Global Alogia</td>
<td>1.1 ± 1.1</td>
<td>1.1 ± 1.1</td>
</tr>
<tr>
<td>SANS Global Avolition</td>
<td>1.7 ± 0.9</td>
<td>2.0 ± 1.0</td>
</tr>
<tr>
<td>SANS Global Anhedonia</td>
<td>1.9 ± 0.9</td>
<td>2.0 ± 1.2</td>
</tr>
<tr>
<td>SANS Global Attention Impairment</td>
<td>1.2 ± 0.9</td>
<td>1.1 ± 1.2</td>
</tr>
<tr>
<td><strong>Mood symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BPRS Anxiety-Depression</td>
<td>5.1 ± 1.2</td>
<td>5.4 ± 3.1</td>
</tr>
</tbody>
</table>

BPRS = Brief Psychiatric Rating Scale; SANS = Schedule for Assessment of Negative Symptoms.

**MOOD SYMPTOMS.** Ratings of mood symptoms (BPRS anxiety-depression did not differ significantly between medication conditions (matched-t values < 1, p = .69), and comprehension accuracy was not associated with anxiety-depression (haloperidol-rho₀₁ = -22, p > .05; placebo-rho₀₁ = .55, p > .02). Moreover, abnormal comprehension performance (T > 60) was not observed more frequently in the patients diagnosed with schizophrenia than in the patients diagnosed with schizoaffective disorder. This latter result was obtained using both the Golden et al (1985) norms (haloperidol-Fisher’s exact test, p = .524; placebo-Fisher’s exact test, p = .733), as well as T scores derived using our normal controls as the standard of comparison (haloperidol-Fisher’s exact test, p = .725; placebo-Fisher’s exact test, p = .363).

**Association between Language Comprehension and Clinical Course**

Measures of clinical course were not associated with comprehension performance during either pharmacologic condition: age at first hospitalization (haloperidol-rho₀₁ = .33, p > .05; placebo-rho₀₁ = -.07, p > .05), duration of illness (haloperidol-rho₀₁ = .13, p > .05; placebo-rho₀₁ = -.12, p > .05), and number of psychiatric hospitalizations (haloperidol-rho₀₁ = -.30, p > .05; placebo-rho₀₁ = .07, p > .05).

Information regarding clinical relapse following haloperidol withdrawal was available for 12 patients, with four patients meeting criteria for exacerbation of psychotic symptoms within 6 weeks of initiating placebo replacement (see criteria above in Haloperidol Maintenance and Placebo Replacement Parent Protocol). Relapse within 6 weeks of haloperidol withdrawal was not associated with abnormal language comprehension performance during either haloperidol maintenance (Fisher’s exact test, p = .575) or placebo replacement (Fisher’s exact test, p = .67), as defined by T > 60 (Golden et al 1985). Relapse was also not associated with change in comprehension accuracy across medication conditions (Fisher’s exact, p = .575).

**Association between Language Comprehension and Pharmacologic Condition**

Haloperidol dose was not associated with language performance (comprehension during haloperidol-rho₀₁ = -.06, p > .05; comprehension during placebo-rho₀₁ = .14, p > .05). Number of days on haloperidol was also not associated with comprehension performance (comprehension during haloperidol-rho₀₁ = .03, p > .05; comprehension during placebo-rho₀₁ = -.27, p > .05). Moreover, number of days placebo was administered prior to testing was not associated with comprehension performance under that condition (rho₀₁ = -.07, p > .05).
Table 5. Mean Cerebrospinal Fluid (CSF) and Plasma Levels of Monoamines in Schizophrenic Patients Evaluated during Haloperidol Maintenance and Placebo Replacement Phases

<table>
<thead>
<tr>
<th></th>
<th>Haloperidol maintenance</th>
<th>Placebo replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CSF</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HVA</td>
<td>[94] ± [23]</td>
<td>[81] ± [63]</td>
</tr>
<tr>
<td>NE</td>
<td>[0.68] ± [0.74]</td>
<td>[0.47] ± [0.20]</td>
</tr>
<tr>
<td>MHPG</td>
<td>[43] ± [14]</td>
<td>[41] ± [16]</td>
</tr>
<tr>
<td>5-HIAA</td>
<td>[81] ± [41]</td>
<td>[89] ± [30]</td>
</tr>
<tr>
<td><strong>Plasma</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HVA</td>
<td>[33] ± [15]</td>
<td>[30] ± [22]</td>
</tr>
<tr>
<td>MHPG</td>
<td>[18] ± [8]</td>
<td>[19] ± [16]</td>
</tr>
</tbody>
</table>

*Each value (parentheses) represents the mean and standard deviation based on 12 subjects except for CSF-MHPG which was based on 11 subjects.

HVA = homovanillic acid; NE = norepinephrine; MHPG = 3-methoxy-4-hydroxyphenylglycol; 5-HIAA = 5-hydroxyindoleacetic acid

**Association between Language Comprehension Performance and CSF and Plasma Monoamines**

Table 5 presents average values of CSF and plasma monoamines of patients during the test week under each pharmacologic condition. These data were not available for all patients. The number of subjects for each measure is noted. Nonsignificant differences were observed in mean levels of CSF monoamines between medication conditions. During placebo replacement, numerical decreases were observed in mean levels of CSF HVA (matched-t1 = 1.38, p = .19), CSF NE (matched-t1 = 1.07, p = .31), and CSF MHPG (matched-t1 < 1, p = .59). A numerical increase was observed in mean level of CSF 5-HIAA (matched-t1 < 1, p = .41). Nonsignificant differences in plasma HVA (matched-t1 = 1.23, p = .24) and plasma MHPG (matched-t1 < 1, p = .87) were also observed between pharmacologic conditions.

Comprehension performance was not associated with CSF or plasma monoamines during either pharmacologic condition: CSF HVA (haloperidol-rho1 = -40, p > .05; placebo-rho1 = -25, p > .05), CSF NE (haloperidol-rho1 = -32, p > .05; placebo-rho1 = .00, p = n.s.), CSF MHPG (haloperidol-rho1 = -42, p > .05; placebo-rho1 = -29, p > .05), CSF 5-HIAA (haloperidol-rho1 = -36, p > .05; placebo-rho1 = -06, p > .05), plasma HVA (haloperidol-rho1 = .19, p > .05; placebo-rho1 = -07, p > .05), and plasma MHPG (haloperidol-rho1 = .005, p > .05; placebo-rho1 = -07, p > .05).

**EFFECT SIZES AND POWER.** Power was determined for alpha = .05, two-tailed. Based on our sample size, observed effect sizes for the group comparisons were large (Cohen 1988). For the comparison of language comprehension performance between patients during haloperidol maintenance and normal controls, a large effect size (d = 1.21) was obtained with a power of .89. For the comparison of comprehension performance between patients during placebo replacement and normal controls, a large effect size (d = 1.42) was also obtained with a power of .96. For the correlation between patients' comprehension performance and anhedonia-asociality, effect size was large (.81) with a power of .98.

For the comparison of patients' comprehension performance during haloperidol maintenance and placebo replacement, a small effect size (d = .17) was observed with a power of .08. Effect size and power were additionally determined for data reported by Plaisted and Golden from their reliability study of the Luria-Nebraska Battery (1982, p. 166). In that reliability study, the difference between the test-retest performance on the Relational Concepts Scale also represented a small effect size (d = .05) and power of .07. Thus, effect size and power of the performance difference between pharmacologic conditions in our present study are highly comparable to the effect size and power obtained in the Plaisted and Golden reliability study in which pharmacologic condition was not manipulated.

**Discussion**

Our findings suggest that language comprehension, as measured by the Luria-Nebraska Relational Concepts scale, is stable in schizophrenia. Previous work has shown that accuracy of language comprehension is reduced in nonpsychotic family members of schizophrenic patients, as compared with normal controls (Condray et al 1992; Hallet and Green 1983), suggesting this cognitive function is associated with familial schizophrenia. However, it was not known whether language comprehension is stable across changes in clinical state, such as during increases in the severity of clinical symptoms or following changes in pharmacologic treatment. Our findings showed patients' comprehension performance to be consistent across pharmacologic conditions, and independent of the positive symptoms of psychosis, mood symptoms, and CSF and plasma monoamines. Patients' comprehension performance was also not correlated with measures of clinical course, level of education, or intelligence.

Our findings are unique and informative, although they should be regarded as preliminary due to small sample size. Several factors, however, increase confidence about the robustness of these initial results. First, our methodology included features associated with a reduction in error variance and an increase in statistical power (see Keppel 1991). We used a repeated measures design in which all patients were evaluated in a controlled double-blind haloperidol maintenance and placebo replacement protocol. Subject selection procedures were designed to produce groups that were as homogeneous as possible, which is also associated with reduced error variance. It should be noted that while repeated measures designs reduce error variance and in-
crease statistical power, a disadvantage is the potential for practice effects on behavioral measures. Interpretation of our results thus requires a balanced consideration of the high test-retest reliability of the Relational Concepts Scale previously demonstrated in psychiatric inpatients (Plaisted and Golden 1982), and the possibility of a performance gain at the second testing that may have confounded the effect of pharmacologic condition in our present study. Counterbalancing of test order and pharmacologic condition is required to address this latter issue definitively. Secondly, analyses of effect size and statistical power based on our results and sample size indicate the phenomena are likely present in the targeted population (Cohen 1988).

The interpretation of patients' significantly reduced comprehension performance warrants careful consideration. Designation of cognitive performance as abnormal or deficient requires some appropriate or meaningful standard of comparison (Lezak 1988). Such standards for schizophrenic patients include the performance of individuals without lifetime psychiatric disorder and individuals with known brain injury. Performance of the majority of our patient group did not fall in the abnormal range when the norms reported by Golden et al (1985) were used as the standard of comparison. Those norms were based on standardization studies that included individuals with general medical conditions and individuals with known brain injury. In contrast, a high proportion of our patient group showed abnormal comprehension performance when the distribution of the normal control group was used as the standard of comparison. Thus, language comprehension in our patient group was not abnormal when compared to a group that included individuals with known brain injury. However, our patient group appeared markedly impaired in this cognitive function when the standard of comparison was a group selected for absence of any lifetime history of psychiatric disorder.

The association observed between comprehension performance and the negative symptom anhedonia-asociality is of interest. Negative symptoms, in general, have been regarded by some investigators as part of an unremitting deficit syndrome, although some evidence suggests that some of these symptoms do fluctuate with medication and state changes (for a review, see van Kammen et al 1991). Anhedonia-asociality, as measured by the SANS instrument (Andreasen 1982), involves a disturbance in the experience of interest or pleasure, and a lack of involvement in social relationships. While patients in the present study did not exhibit a significant increase in anhedonia-asociality during haloperidol maintenance, the number of their comprehension errors was significantly associated with the severity of this clinical symptom under this pharmacologic condition. Language comprehension and language production likely involve both overlapping and different cognitive functions. Therefore, comments comparing and contrasting the findings from studies that address these two domains should be viewed with that qualification. Thus, our finding of an association between patients' comprehension and the negative symptom anhedonia-asociality is generally consistent with previous studies showing associations between presence of negative symptoms and reductions in syntactic complexity of speech in schizophrenic patients (Thomas et al 1987; 1990). In our study, the association between language comprehension and negative symptomatology was observed only during haloperidol maintenance, which suggests that the relationship between language comprehension and negative symptomatology may be influenced by pharmacologic treatment.

Language comprehension was not correlated with positive symptoms of psychosis, with anxiety-depression, or with measures of clinical course including age at first hospitalization, duration of illness, number of psychiatric hospitalizations, and clinical exacerbation within 6 weeks of haloperidol withdrawal. Again, although language understanding and production likely involve both common and distinct cognitive functions, independence of language comprehension and positive symptoms of psychosis in our present study is generally consistent with results reported by Morice and Ingram (1983) who found a lack of association between psychotic symptoms and the syntactic complexity of patients' speech. Those investigators also observed an association between age of onset of illness and syntactic complexity of speech (Morice and Ingram 1983), which contrasts to our present finding of no association between patients' comprehension and age at first hospitalization. This latter distinction suggests that language comprehension and language production in schizophrenia may involve different relationships with age of onset of disorder.

What cognitive processes might account for the disturbance in language comprehension in schizophrenic patients? Our data showed independence between patients' Relational Concepts performance and their level of education and intelligence, including short-term memory function. These results are consistent with previous findings. In a study conducted by Goldstein and Shelly (1984), language and verbal intelligence were measured in a large sample of neuropsychiatric patients, and the data were entered into a factor analysis. Among the various tests used were the WAIS Verbal subtests and the Luria-Nebraska Factor Scales, including the Relational Concepts Scale. Results showed that the verbal intelligence tests and the Relational Concepts Scale loaded on two separate or independent factors, which were labelled as Verbal Intelligence and Comprehension of Syntactical Relations, respectively. Moreover, age and education were not related to the comprehension factor in this study by Goldstein and Shelly. Thus, our finding of no association between schizophrenic...
patients' language comprehension and their intelligence and educational level is consistent with previous findings for a large sample of neuropsychiatric patients.

Independence of language comprehension from intelligence and level of education may be due to the nature of language comprehension as it is measured by the Relational Concepts Scale. Intelligence and educational achievement are generally regarded as components of overall neuropsychological functioning, but these components are not expected to be associated with performance on all cognitive tasks (see McKay and Golden 1981; Goldstein and Shelly 1984; Shelly and Goldstein 1982). Luria's concept of "functional systems" (1980, 1973) may be germane to this issue. According to Luria's view of higher neuropsychological processes, performance of complex tasks is accomplished through integration of a number of basic neuropsychological functions that may vary in number and type across tasks. More specifically, processes engaged during sentence comprehension may represent such a "functional system" that accomplishes what Luria described as "a special form of synthesis of the individual elements, in which the consecutive scrutiny of these elements is transformed into a simultaneous operation (1980, p. 500)." An item from the Relational Concepts Scale provides an example: "Arnie hit Tom. Who was the victim?" Understanding that Tom is the object of the action directed by Arnie requires an analysis that goes beyond mere word comprehension; namely, determining the syntactic relationships between sentence constituents which are specified by the word order of the sentence [viz: SUBJECT<sub>noun</sub>, VERB<sub>noun</sub>, OBJECT<sub>noun</sub>]. Luria's formulation of sentence comprehension as a unique operation receives support from the neuropsychological literature (e.g., Goldstein and Shelly 1984).

In summary, we examined the language comprehension performance of schizophrenic patients who were tested during a controlled double-blind haloperidol maintenance (no anticholinergic medications) and placebo replacement protocol. Patients' comprehension, measured by the Luria-Nebraska Relational Concepts Scale, was significantly reduced under both pharmacologic conditions, compared with normal controls. More importantly, patients' language performance did not differ significantly between medication conditions. Performance was also not associated with haloperidol dose, or with amount of time that haloperidol and placebo were administered prior to testing. Patients' comprehension performance was independent of the positive symptoms of psychosis, mood symptoms, and indicators of clinical course. Patients' language performance was also not correlated with CSF and plasma monoamines. Furthermore, patients' comprehension accuracy was not associated with intelligence or level of education. Comprehension accuracy was significantly associated only with the negative symptom anhedonia-asociality during haloperidol maintenance.

The findings of our present study provide information about the stability of a specific language capacity across changes in the state of schizophrenic patients. In this sample, the aspects of language comprehension that are assessed by the Luria-Nebraska scale conform to the characteristics of a trait phenomenon. That is, patients' performance on this scale was resistant to the effects of state dynamics that are associated with changes in antipsychotic medication and positive symptoms of psychosis. Whether additional dimensions of language comprehension also show trait features in this psychiatric population is an open empirical question, and we are presently evaluating this possibility in an ongoing study. Thus, in our present study, language comprehension performance in schizophrenic patients was consistent with the notion of a psychological trait that shows stability across time and across variations in state (e.g., Depue et al 1994; Haan et al 1986; Pervin 1984).

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