Neurocognitive Vulnerability, Interpersonal Criticism, and the Emergence of Unusual Thinking by Schizophrenic Patients During Family Transactions

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Background: This study examined whether the combination of patients’ neurocognitive deficits and criticism by others would predict the emergence of patients’ unusual thinking during stressful family transactions.

Methods: When clinically stable, 41 patients with recent-onset schizophrenia completed 2 versions of a visual vigilance task, the Continuous Performance Test (CPT). One CPT emphasized early perceptual processing, while the other stressed immediate, working memory. On a separate occasion, patients and family members participated in a 20-minute interaction in which the number of relatives’ criticisms and patients’ unusual thoughts was assessed.

Results: In a hierarchical regression model, after entering performance on the CPT demanding immediate, working memory, and the number of criticisms by family members, the interaction of CPT performance and criticism significantly predicted the number of patients’ unusual thoughts during the family session ($r^2$ change = 0.09; $P = .03$). Post hoc analyses revealed that the number of criticisms and odd thoughts correlated significantly ($r = 0.59$, $P = .03$) for patients who had poor memory-load CPT performance, but were unrelated ($r = -0.07$) for patients who did well on the memory-load CPT. The CPT emphasizing early visual processing, either alone or in combination with interpersonal criticism, did not predict the number of patients’ unusual thoughts during the interaction.

Conclusion: The results suggest that the combination of patients’ working memory deficits and interpersonal criticism jointly predicts psychotic thinking, consistent with a model of schizophrenia that emphasizes the interaction of neurocognitive vulnerability and psychosocial stress factors.

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Several models of schizophrenia hypothesize that the exacerbation of psychotic symptoms involves the interaction of psychobiological vulnerability factors and environmental stressors.1-6 One such viewpoint, a heuristic vulnerability stress model,7,8 further hypothesizes that there are 2 types of enduring vulnerability factors in schizophrenia. Stable vulnerability factors reflect indicators of proneness to develop the disorder. Mediating vulnerability factors also indicate a proneness to develop the disorder, but, in addition, predict and mediate the emergence of symptoms in individuals who already have the disorder.7,8

Initial evidence suggests that early perceptual processing deficits reflect a stable vulnerability factor in schizophrenia, whereas a disturbance in immediate, working memory may be a vulnerability factor that mediates symptom formation. Earlier analyses from our project8,9 examined neurocognitive performance of 17 patients with recent-onset schizophrenia during both psychotic and remitted clinical states. Two versions of the Continuous Performance Test (CPT) were administered, both involving the presentation of a quasi-random series of single digits flashed briefly at a pace of 1 per second. In a degraded-stimulus CPT, early perceptual processing was emphasized by blurring the digits and asking patients to detect each blurred “0.” In a memory-load CPT, working memory was stressed by asking patients to detect occasions on which a sequence of digits occurred (“3” followed by “7”) in a series of clearly focused single digits.

Patients with schizophrenia performed significantly worse than matched normal controls in both remitted and psychotic states when early perceptual processes were emphasized. More importantly, performance in this situation was
PARTICIPANTS AND METHODS

PARTICIPANTS

Forty-one patients with recent-onset schizophrenia and their family members participated in this study. Patients and key relatives were recruited for a longitudinal study of the early course of schizophrenia. Patients and their relatives were provided oral and written information about the project and signed informed consent agreements. Patients were recruited from 4 hospitals in the Los Angeles area. Criteria for patient admission into the longitudinal study included (1) a diagnosis of schizophrenia or schizoaffective disorder, mainly schizophrenic, by Research Diagnostic Criteria; (2) first onset of major psychosis no more than 2 years before first project contact; (3) age between 18 and 45 years; and (4) no known neurological disorder, recent significant and habitual substance abuse, or premorbid mental retardation. Diagnoses were based on an expanded version of the Present State Examination (PSE) administered to the patient with additional information obtained, as needed, from family members. Minimum interrater agreement between PSE interviewers and a criterion rater before interviewing patients for the study was 85% for the presence of symptoms related to the diagnosis of schizophrenia, and 95% agreement on the absence of items relevant to the diagnosis. Rater drift was also monitored throughout the study to ensure that raters continued to meet these criteria.

Schizophrenia patients in this sample ranged in age from 18 to 32 years (mean [SD] age, 22.5 [3.6] years). Patients were predominantly male (37 men and 4 women), Caucasian (35 Caucasians, 3 Hispanic Americans, 1 Asian American, and 2 of mixed race), and from all social classes (mean [SD] socioeconomic status, 2.9 [1.1] based on the 5-point Hollingshead Index of Social Position). Their mean (SD) educational level was 12.6 (1.8) years (range, 9-16 years). Patients had been ill, including prodromal symptoms, a mean (SD) of 16.3 (10.9) months (range, 1-53 months) at the time of their initial participation in the study.

PROCEDURE

Neurocognitive Tasks

Patients were presented with 2 versions of the CPT, a measure of visual vigilance or sustained attention. Both versions assessed the ability to detect target numerals presented in a rapidly paced sequence. The degraded-stimulus version measures early perceptual processing abilities, whereas the memory-load version assesses patients’ ability to hold a prior stimulus in memory and use it as a cue to guide response to the current stimulus. Stimuli were presented at a pace of 1 digit per second with 40-millisecond exposures using an electronic shutter and rear projection system. Numbers were 6.3 cm high and 4.8 cm wide and viewed from 1 m. Patients were instructed to press a button held in their dominant hand as quickly as possible whenever the target stimulus appeared. They were told that it was important to respond to targets as well as to avoid pressing the button for nontargets. For each CPT task, the proportion of target detections (hit rate) and the percentage of responses to nontargets (false-alarm rate) was recorded. Order of tasks was counterbalanced across subjects and for each CPT task, the dependent variable was the d’ level, the signal/noise discrimination index that is independent of tendencies to respond liberally or conservatively to stimuli that might be targets.

Both tasks were administered to patients after they had been clinically stabilized and maintained on a stable dose of fluphenazine decanoate (usually 12.5 mg every 2 weeks) for 1 month. Antiparkinsonian medication was temporarily interrupted 48 hours before testing in 28 of 41 patients. One patient was not administered the memory-load CPT as this test was developed after the patient’s testing session.

Degraded-Stimulus CPT

The adult version of the degraded-stimulus CPT was used. The single digits 0 through 9 were degraded by blurring to the extent that they required a 2.8-diopter lens correction to refocus. Patients were instructed to respond whenever the digit 0 was presented. After a 2.7-minute practice session, 120 target and 366 nontarget stimuli were administered in quasi-random order (identical digits never followed one another and digits preceding 0 were balanced) over an 8.1-minute period.

Memory-Load CPT

In this variant of the A-X CPT, patients were told to respond whenever a 3 preceded a 7 in a series of clearly focused single digits. Nontargets included other digits as well as 3s and 7s not in the 3 to 7 sequence. After a 2.45-minute practice session, 80 target and 568 nontarget sequences were presented quasi-randomly over a 10.8-minute period. Because a sequence of 2 stimuli is required for each target, this task was longer than the degraded-stimulus CPT to allow sufficient target stimuli for reliable calculation of d’ level.

Continued on next page
whether working memory performance in a laboratory setting when patients were stable would predict the emergence of subclinical psychotic symptoms during stressful family transactions.

The second purpose of the study was to examine whether psychosocial stressors would interact with neurocognitive deficits to predict the emergence of subclinical psychotic symptoms. Research has shown that high levels of criticism, hostility, and/or emotional involvement among relatives of patients with schizophrenia within family transactions. The Patient Symptom Profile is based, in part, on dimensions from the expanded Brief Psychiatric Rating Scale and the Schedule for Affective Disorders and Schizophrenia.

The Patient Symptom Profile individual code for unusual thinking was chosen as the dependent measure in this study because this variable directly assesses clinical and subclinical psychotic symptom dimensions. Furthermore, this code was based directly on the Brief Psychiatric Rating Scale item, unusual thought content, which contributed to the determination of psychotic relapse in the associated longitudinal study. This measure assesses any instance of odd, strange, or bizarre thought content (eg, “If that kid bites you, you’ll get rabies”). Coding was based solely on speech content, not on whether speech was disorganized.

In previous research, unusual thinking by patients during the interaction was found to correlate significantly with current symptom levels on the thought disturbance factor of the Brief Psychiatric Rating Scale. Within the current sample, this variable significantly differentiated patients from high vs low expressed-emotion environments. Unusual thinking during a baseline family interaction has also been shown to predict relapse in bipolar disorder.

The unit of analysis was each speech segment. The unit ended when a relative either responded to or interrupted the patient. The dependent variable was the total number of unusual thoughts expressed by the patient over the two 10-minute interactions. Each transcript was coded by the first author (I.S.R.), who was blind to family expressed emotion or affective style data and patient neurocognitive performance. After training, an advanced undergraduate also rated 30 transcripts from this sample. Interrater reliability for the 2 coders for unusual thinking was 0.73 (Cohen κ, P = .01).

STATISTICAL ANALYSES

Data were examined through 2 hierarchical, multiple regression analyses. The first analysis examined whether the hypothesized stable vulnerability factor, degraded-stimulus CPT d', and number of interpersonal criticisms, would significantly predict frequency of patients’ unusual thinking during the family interaction. Degraded-stimulus CPT scores were entered first, interpersonal criticism second, and the interaction term last. In the second equation, the hypothesized mediating vulnerability factor, memory-load CPT d' was entered first, interpersonal criticism second, and the interaction of memory-load CPT d' and criticism last. For all analyses, α was set at P < .05.
show in a relatively remitted clinical state interacts with the amount of interpersonal criticism experienced to affect the occurrence of unusual thinking by patients. Furthermore, we hypothesized that perceptual processing deficits, which seem to represent a stable vulnerability factor in schizophrenia, would not be associated with emergence of subclinical psychotic symptoms during a stressful family transaction.

**RESULTS**

Table 1 shows means and SDs for all measures. The first analysis examined whether degraded-stimulus CPT \( d' \) and number of interpersonal criticisms would significantly predict patients’ unusual thinking. Results indicated that only interpersonal criticism added significantly to the regression model \( (r^2 \text{ change}=0.12; P=.02) \) (Table 2). Consistent with expectations for a stable vulnerability factor, the interaction term failed to add significantly to the equation \( r^2 \text{ change}=0.02; P=.38 \). In the second analysis, memory-load CPT \( d' \) did not significantly predict patients’ unusual thinking \( (F_{1,38}=2.66; P=.11) \). The addition of interpersonal criticism did add significantly to the model \( (r^2 \text{ change}=0.15; P=.01) \), and at step 3, the interaction term also contributed significantly \( (r^2 \text{ change}=0.09; P=.03) \). The complete model accounted for 31% of the variance in patients’ unusual thinking (see Table 3 for the complete regression model).

To determine the nature of the interaction, Pearson correlations and scatterplots were used to examine the relationship between interpersonal criticism and unusual thinking among high (top one third) and low (bottom one third) performers on the memory-load CPT. As can be seen in the Figure, for patients performing in the top third \( (n=13) \) on the memory-load CPT, the correlation between the number of criticisms expressed and patients’ unusual thinking was \( r = -0.07 \). For patients performing in the bottom third \( (n=13) \) on the memory-load CPT, however, the correlation between the number of criticisms expressed and patients’ unusual thinking was \( r = 0.59 \) (\( P=.03 \)). One patient’s data were excluded from the bottom third group because he scored more than 2 SDs above the mean on unusual thinking. With this patient’s data included in the analysis, the correlation between criticism and odd thinking for patients scoring in the bottom third on the memory-load CPT was \( r = 0.84 \) (\( P<.0001 \)).

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hit rate</td>
<td>0.60 (0.23)</td>
</tr>
<tr>
<td>FA rate</td>
<td>0.07 (0.09)</td>
</tr>
<tr>
<td>Reaction time (in milliseconds), hits</td>
<td>610.24 (101.13)</td>
</tr>
<tr>
<td>Reaction time (in milliseconds), FA</td>
<td>626.71 (113.48)</td>
</tr>
<tr>
<td>( d' )</td>
<td>2.00 (1.10)</td>
</tr>
<tr>
<td>Memory-load CPT (n = 40)</td>
<td></td>
</tr>
<tr>
<td>Hit rate</td>
<td>0.83 (0.18)</td>
</tr>
<tr>
<td>FA rate</td>
<td>0.00 (0.01)</td>
</tr>
<tr>
<td>Reaction time (in milliseconds), hits</td>
<td>461.51 (93.38)</td>
</tr>
<tr>
<td>Reaction time (in milliseconds), FA</td>
<td>550.47 (250.02)</td>
</tr>
<tr>
<td>( d' )</td>
<td>3.83 (0.90)</td>
</tr>
<tr>
<td>No. of family criticisms</td>
<td>4.24 (5.89)</td>
</tr>
<tr>
<td>No. of unusual thoughts expressed</td>
<td>2.73 (4.53)</td>
</tr>
</tbody>
</table>

* FA indicates false alarm; \( d' \) indicates a signal/noise discrimination index.
† Family criticism and unusual thinking scores are added across the two 10-minute interactions.

**Table 2. Hierarchical Multiple Regression Using Degraded-Stimulus Continuous Performance Test (CPT) \( d' \) and Interpersonal Criticism to Predict Unusual Thinking by 41 Patients**

<table>
<thead>
<tr>
<th>Step/Predictor Variable</th>
<th>( R )</th>
<th>( R^2 ) Change</th>
<th>( R^2 )</th>
<th>F, Change (df)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/ degraded-stimulus CPT ( d' )</td>
<td>0.11</td>
<td>0.01</td>
<td>0.01</td>
<td>0.47 (1,39)</td>
</tr>
<tr>
<td>2/ interpersonal criticism</td>
<td>0.36</td>
<td>0.12</td>
<td>0.13</td>
<td>5.26† (1,38)</td>
</tr>
<tr>
<td>3/ degraded-stimulus CPT ( d' ) × interpersonal criticism</td>
<td>0.39</td>
<td>0.02</td>
<td>0.15</td>
<td>0.76 (1,37)</td>
</tr>
</tbody>
</table>

* \( d' \) indicates a signal/noise discrimination index.
† \( P<.05 \).

Scatterplot of the relationship between the number of criticisms expressed by family members during a family interaction and the number of unusual thoughts expressed by patients with recent-onset schizophrenia during the family transaction, as a function of the memory-load Continuous Performance Test (CPT) performance of the patient. Those patients scoring in the bottom one third \( (n=13) \) on the memory-load CPT are on the left side; those scoring in the top one third \( (n=13) \) on the memory-load CPT are on the right side. The presence of memory-load CPT deficits interacts with interpersonal criticisms to predict expression of unusual thinking by patients with schizophrenia.
The results indicate, as hypothesized, that the combination of deficits in immediate, working memory in patients with recent-onset schizophrenia, as evidenced by memory-load CPT performance in a stabilized outpatient state, and interpersonal criticism directed toward the patient by relatives is associated with the emergence of unusual thinking by patients during stressful family transactions. The data also indicate that early perceptual processing deficits, when assessed either alone or in combination with interpersonal criticism directed toward the patient, are not associated with the emergence of subclinical psychotic symptoms during stressful family transactions. Thus, these data add further empirical support to prior research,8,9 which suggested that active working memory processing deficits in schizophrenia may serve as a mediating vulnerability factor in the escalation of schizophrenia symptoms.

It is important to point out, however, that reduced working memory capacity, in isolation, was not associated significantly with patients’ unusual thinking in this study. Instead, these data suggest that working-memory deficits in schizophrenia might be associated with the tendency toward psychotic thinking when interpersonal stessors occur. These results underscore the importance of examining psychosocial stressors when determining whether patient neurocognitive vulnerability factors are associated with the escalation of subclinical symptoms.

The data also underscore the importance of considering the severity of patients’ neurocognitive deficits when determining whether psychosocial stress exacerbates symptoms. Interpersonal criticism had little relationship to patients’ unusual thinking unless patients also had reduced active memory capabilities. Thus, patients’ neurocognitive deficits may determine whether interpersonal stress potentiates psychotic thinking.

It is noteworthy that patient performance on the degraded-stimulus CPT was not associated with the escalation of subclinical psychotic symptoms in patients with recent-onset schizophrenia. Research has indicated that patients with schizophrenia perform significantly worse than nonpsychiatric subjects on this task8,20,30 as well as on similar neurocognitive tasks that assess early visual information-processing skills.31,32 First-degree relatives of patients with schizophrenia also perform worse on these tasks than subjects with no known relatives with schizophrenia.21,33-35 Our results are consistent with prior research that has indicated that these early perceptual processing deficits are indicators of vulnerability to develop schizophrenia but may not be direct factors in the escalation of symptoms within patients who already have the disorder.8,9

This study is limited by its focus on patient subclinical symptoms during stressful family transactions. Although prior research found that these symptoms correlate significantly with patients’ psychotic symptoms on the Brief Psychiatric Rating Scale,22 additional research is needed to determine whether the interaction of working-memory deficits and interpersonal criticism is also associated with increasing the probability of a subsequent psychotic relapse. We also cannot rule out the possibility that criticism by others was partially a consequence of, rather than a predictor of, patients’ unusual thinking during the interaction. In prior analyses, however, we have found that while interpersonal criticism in high expressed-emotion families occurs in reaction to the first unusual thought by patients, it is also associated with an increased probability of subsequent unusual thinking by the patient.24

The data provide further evidence of the importance of distinguishing between neurocognitive vulnerability factors in schizophrenia that play a immediate role in symptom formation and those that indicate stable proneness to develop the disorder.7 The results also provide empirical support for a vulnerability stress interaction in schizophrenia—the emergence of odd or unusual thinking is best accounted for by considering the interacting effects of a neurocognitive vulnerability factor and a psychosocial stressor.

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