Use of Methods From Chaos Theory to Quantify a Fundamental Dysfunction in the Behavioral Organization of Schizophrenic Patients

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Objective: This study aimed to quantify the complexity of behavioral sequences of patients with schizophrenia and comparison subjects by using methods from nonlinear dynamical systems theory. Method: A simple choice task consisting of predicting 500 random right or left appearances of a stimulus was used to obtain binary response sequences in 22 patients with schizophrenia and 16 comparison subjects. Dynamical entropy was measured and the fluctuation spectrum of local subsequence entropies calculated to quantify the degree of interdependency between consecutive responses of patients and comparison subjects. Results: The response sequences generated by the schizophrenic patients exhibited a higher degree of interdependency than those of comparison subjects. Moreover, schizophrenic patients exhibited significantly less consistency in their response selection and ordering, characterized by a greater contribution of both highly perseverative and highly unpredictable subsequences of responses within a test session. Conclusions: The result of the biological abnormality underlying schizophrenia may not be a simple increase or decrease of neuropsychological or neurobiological functions. Instead, the observed abnormalities in behavioral patterns reflect a quantifiable dysregulation and disorganization of these functions.


A wide range of experimental paradigms based on information processing and neurobiological, neuroadaptive, and neuropsychological strategies and theories have been used to study the fundamental dysfunctions underlying schizophrenia (1–4). These investigations indicate that schizophrenic dysfunction can be conceptualized as deficient formation of adaptive behavioral patterns resulting from inappropriate selection, ordering, and sequencing of behavioral elements. Advances in nonlinear dynamics (5) provide techniques that enable researchers to quantify these dysregulated behavioral patterns. Measures derived from chaos theory have been applied in order to quantify patterns of biological and physical phenomena ranging from EEG to weather dynamics (6–8). Specifically, these methods quantify not only the average interdependency between observations within a sequence but also the contribution of different degrees of interdependencies for subsequences of observations. Therefore, these techniques can be used to comprehensively quantify the organization of behavioral sequences on a microscopic or subsequence and macroscopic or average level. These methods may be particularly valuable for assessing schizophrenia, which has been hypothesized to constitute a complex dysregulation of neurobiological (9) and behavioral (10) systems rather than a simple up- or down-regulation.

Thought disorder, a central characteristic of schizophrenia (11), can be conceptualized as a failure to put thoughts and perceptions into their proper relationships. Although usually measured by means of interviews and cognitive tasks, the organization of thought processes can also be assessed by using paradigms involving the subject’s thought-contingent responses. Experimentally, a choice task with two response alternatives can assess the thought-contingent formation of response patterns that are viewed as analogous to the assessment of the subject’s perceptual patterns and ego impairment (12).

Studies using choice tasks have revealed that although some patients with schizophrenia displayed reduced response variability (13, 14), those with predominantly negative symptoms exhibited excessive alternations. Stud-
ies using binary choice tasks have also revealed that intellectually impaired patients with chronic schizophrenia showed single-response perseveration (15). Thus, schizophrenic patients exhibit patterns of responding that are distinct from those of comparison subjects. In order to precisely quantify these patterns, we used a simple behavioral paradigm combined with a nonlinear analysis technique to test the hypothesis that schizophrenic patients generate both “perseverative tendencies” and highly “chaotic” response patterns. Most important, we hypothesized that extremes of highly predictable and highly unpredictable response patterns would occur within each individual subject and not in a subgroup of highly perseverative responders or a subgroup of highly “chaotic” responders.

**METHOD**

Twenty-two patients with schizophrenia and 16 comparison subjects were tested. The patients were diagnosed according to Research Diagnostic Criteria (16) and included 13 inpatients and nine outpatients, 15 men and seven women, with a mean age of 33.6 years (SD=2.0), a mean duration of illness of 13.6 years (SD=1.98), a mean of 51 hospitalizations (SD=1.0), and a mean treatment regimen of 75.9 mg/day in chlorpromazine equivalents (SD=172.4). Normal comparison subjects included nine men and seven women whose mean age was 27.4 years (SD=2.8) who were recruited from a San Diego State University undergraduate basic psychology course or from a well-screened control group selected for participation in a clinical research center study. Two patients and one comparison subject were excluded from the analysis because of incomplete data sets. All participating subjects provided written informed consent.

For the choice task paradigm, subjects sat in front of a monitor and were given a small device (trackball) with left and right buttons. The explanation of the task was shown on the monitor; the experimenter answered any questions. The task consists of repeatedly predicting whether an object (a car) will appear on the left or the right side of the display. The location is selected randomly by the computer. The experiment consists of 500 trials. Each trial is initiated by the subject’s selecting the left or right button and terminated by the object’s flashing briefly (250 msec) on either side. For each trial, the response of the subject (0=left, 1=right), the between-response time (in milliseconds), and the computer-generated location (left or right) are recorded and stored on the computer.

Similar to our analysis of dynamical patterns in the locomotor behavior of animals (17), the sequences of the subjects’ binary responses were analyzed by a nonlinear dynamical technique that quantifies the interdependency between consecutive responses; details of this technique are given elsewhere (18). Dynamical entropy, or h, measures the extent to which the next response cannot be predicted by the previous responses; h=0 if the subject’s next response can be completely predicted from the subject’s current response and h=1 if the next response cannot be predicted. Moreover, h can be greater than 1 if the next response cannot be predicted from several previous responses. The thermodynamic formalism of dynamical systems (5, 19, 20) provides a quantitative framework to assess the within-subject variation of this interdependency by determining the frequency of local dynamical entropies that are defined for subsequences of responses. The degree of interdependency is related to the response subgroup length that uniquely identifies a subsequence of responses within a sequence. Long subsequence lengths identify highly interdependent (more predictable) responses, whereas short subsequence lengths indicate highly independent (unpredictable) responses.

Computationally, the response sequence is divided into unique subsequences of responses that are stored as branches in a complexity tree (18). The logarithm of the number of responses divided by the average branch depth of the complexity tree yields the average dynamical entropy. Local dynamical entropies are calculated from the depths of the individual branches of the complexity tree. The fluctuations of local dynamical entropies are quantified by the fluctuation spectrum of local dynamical entropies and calculated from the distribution of branch depths in the complexity tree. This function corresponds to the logarithm of the occurrence rate for a branch with a specific local entropy. In addition, the probability of a switch response (two consecutive choices of the type “01” (left-right) or “10” (right-left), response balance (i.e., the number of right choices minus the number of left choices), and the average between-response interval were used to assess qualitative characteristics of the response sequences.

**RESULTS**

Differences between the 20 schizophrenic patients and the 15 comparison subjects in scores on psychiatric symptom scales (the Brief Psychiatric Rating Scale [BPRS], Scale for the Assessment of Negative Symptoms, and Scale for the Assessment of Positive Symptoms) and in the overall choice task measures (dynamical entropy, response switching, response balance, and response duration) were assessed by using t tests with the Welch approximation for unequal variances (21). Table 1 summarizes the results for the psychiatric assessment and the overall choice task measures. As expected, patients with schizophrenia had significantly more positive and negative symptoms as well as higher total BPRS scores and higher scores on the BPRS thought disorder subscale than the comparison subjects.

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**Table 1.** Scores of 20 Patients With Schizophrenia and 15 Normal Comparison Subjects on Psychiatric Tests and Overall Choice Task Measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Schizophrenic Patients</th>
<th>Comparison Subjects</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Psychiatric test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scale for the Assessment of Positive Symptoms</td>
<td>35.56</td>
<td>21.80</td>
<td>0.69</td>
</tr>
<tr>
<td>Scale for the Assessment of Negative Symptoms</td>
<td>35.60</td>
<td>16.30</td>
<td>0.84</td>
</tr>
<tr>
<td>Brief Psychiatric Rating Scale</td>
<td>28.60</td>
<td>11.70</td>
<td>3.76</td>
</tr>
<tr>
<td>Brief Psychiatric Rating Scale thought disorder subscale</td>
<td>11.08</td>
<td>5.90</td>
<td>0.38</td>
</tr>
<tr>
<td>Overall choice task measure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dynamical entropy (h)</td>
<td>0.46</td>
<td>0.16</td>
<td>0.55</td>
</tr>
<tr>
<td>Switching</td>
<td>0.37</td>
<td>0.15</td>
<td>0.38</td>
</tr>
<tr>
<td>Balance</td>
<td>0.01</td>
<td>0.28</td>
<td>0.00</td>
</tr>
<tr>
<td>Duration</td>
<td>698.13</td>
<td>672.30</td>
<td>455.24</td>
</tr>
</tbody>
</table>

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The average dynamical entropy, $h$, differed significantly between schizophrenic patients and comparison subjects, indicating that, on the average, the responses of schizophrenic patients are more predictable. In contrast, the schizophrenic patients did not differ significantly from the comparison subjects in probability of response switches, response balance, or response duration, indicating that the patients were not simply aberrant on all measures. Although both schizophrenic patients and comparison subjects tended to switch responses less frequently than would be predicted by chance, no preferences were found for either the left or the right response alternative for either group.

As shown in figure 1(a), the group fluctuation spectrum of local dynamical entropies for schizophrenic patients, $S_i(h)$, envelops the $S_i(h)$ for comparison subjects, indicating more varied response patterns. These curves reveal that schizophrenic patients generated more subsequences that are highly interdependent (low local dynamical entropy) and more subsequences that are highly unpredictable (high local dynamical entropy) than did normal comparison subjects. The significance of these differences is quantified by the difference $t$ scores, $S_i(h)$, shown in figure 1(b). Subsequences having low ($h < 0.3$) and high ($h > 0.7$) local dynamical entropies contributed significantly more to differences in the overall response sequence between schizophrenic patients and comparison subjects. The individual local dynamical entropies function, $S(h)$, of two representative subjects from each group is shown in figure 1(c). Thus, the enveloping $S(h)$ function was not due to subgroups of schizophrenic patients with either highly predictable or highly unpredictable response sequence but, rather, reflected the greater contribution of both subsets for individual patients. These difference scores indicate that a bifurcation of the contribution of subsequences corresponds to the fundamental dysfunction in behavioral organization for schizophrenic patients relative to comparison subjects.

CONCLUSIONS

The use of the binary choice task provides a simple behavioral paradigm to measure interdependencies between consecutive behavioral responses. The application of nonlinear methods in general, and the fluctuation spectrum analysis of local dynamical entropies in particular, supplies a quantitative framework to examine the composition of these behavioral responses. This approach enables a comprehensive quantitative assessment of sequential response organization. In particular, this analysis not only gauges higher or lower rates of a behavioral response but also quantifies patterns of dysregulations that are characterized by distinct compositions of behavioral responses (18).

The results suggest that patients with schizophrenia exhibit complex patterns of dysregulation rather than a simple up- or down-regulated predictability of response patterns. First, on the average, response sequences generated by schizophrenic patients were more predictable or interdependent than the sequences generated by comparison subjects. This result is in agreement with findings that schizophrenic patients are characterized by less complex neurobehavioral measures than normal subjects. For example, using a nonlinear approach, Roschke and Aldenhoff (22) reported reduced dimensionality of the EEG during sleep stages II and REM for schizophrenic patients than for comparison subjects (22). Moreover, Hoffman et al. (4) found that schizophrenic patients exhibited a high degree of semantic recurrence in hallucinated "voices" reported during a listening task.

Second, the qualitative characteristics of sequences
measured by the response switching, response balance, and between-response duration did not differ significantly between groups. It is crucially important to note that the differential change in the sequence complexity, without observed changes in the qualitative characteristics of the sequences, indicates a circumscribed rather than a general deficit in sequential organization in schizophrenic patients.

Third, the fluctuation spectrum of local dynamical entropies for the response subsequences generated by schizophrenic patients was more diverse than the spectrum of comparison subjects—figure 1(a) and figure 1(b)—and the spectra of individual patients were more diverse than those of individual comparison subjects—figure 1(c). Specifically, individual schizophrenic patients exhibited both highly interdependent and highly unpredictable response subsequences, but individual comparison subjects generated relatively uniform response subsequences having intermediate entropy values. Most importantly, the different shapes of the fluctuation spectra cannot be explained by interindividual differences (e.g., subgroups with highly interdependent or highly unpredictable subsequences). Instead of an overall increase or decrease of interdependency in the response sequences, the dysregulation of the response organization of schizophrenic patients is characterized by a fluctuation between subsequences with highly varying degrees of interdependencies.

In conclusion, the use of fluctuation spectrum analysis and other nonlinear methods to provide detailed quantitative assessment of the sequential response organization is likely to provide a better understanding of the complex dynamical dysregulation of clinical, cognitive, and neurobiological processes underlying schizophrenia.

REFERENCES