The Nonlinear, Complex Sequential Organization of Behavior in Schizophrenic Patients: Neurocognitive Strategies and Clinical Correlations

Martin P. Paulus, William Perry, and David L. Braff

Background: *Thought disorder is a hallmark of schizophrenia and can be inferred from disorganized behavior. Measures of the sequential organization of behavior are important because they reflect the cognitive processes of the selection and sequencing of behavioral elements, which generate observable and analyzable behavioral patterns. In this context, sequences of choices generated by schizophrenic patients in a two-choice guessing task fluctuate significantly, which reflects an "oscillating dysregulation" between highly predictable and highly unpredictable subsequences within a single test session. In this study, we aimed to clarify the significance of dysregulation by seeing whether demographic, clinical, neuropsychological, and psychological measures predict the degree of dysregulation observed on this two-choice task.*

Methods: *Thirty schizophrenic patients repeatedly performed a LEFT or RIGHT key press that was followed by a stimulus, which occurred randomly on the left or right side of the computer screen. Thus, the stimulus location had nothing to do with the key press behavior. The range of key press sequence predictabilities as measured by the dynamical entropy was used to quantify the dysregulation of response sequences and reflects the range of fixity and randomness of the responses. A factor analysis was performed and step-wise multiple regression analyses were used to relate the factor scores to demographic, clinical, symptomatic, Wisconsin Card Sorting Test (WCST), and Rorschach variables.*

Results: *The LEFT/RIGHT key press sequences were determined by three factors: 1) the degree of win-stay/lose-shift strategy; 2) the degree of contextual influence on the current choice; and 3) the degree of dysregulation on the choice task. Demographic and clinical variables did not predict any of the three response patterns on the choice task. In contrast, the WCST and Rorschach test predicted performance on various factors of choice task response patterns.*

Conclusions: *Schizophrenic patients employ several rules, i.e., "win-stay/lose-shift" and "decide according to the previous choice," that fluctuate significantly when generating sequences on this task, confirming that a basic behavioral dysregulation occurs in a single schizophrenic subject across a single test session. The organization or the "temporal architecture" of the behavioral sequences is not related to symptoms per se, but is related to deficits in executive functioning, problem solving, and perceptual organizational abilities.* Biol Psychiatry 1999;46: 662–670 *© 1999 Society of Biological Psychiatry*

Key Words: Sequential organization, choice behavior, neurocognition, nonlinear dynamics, schizophrenia

Introduction

Schizophrenia is a complex disorder that affects a wide array of psychological functions. Historically, these functional disturbances have been conceptualized as arising from a "fundamental" deficit in attention (e.g., Bleuler 1950). More recently, investigators have described the fundamental deficit in schizophrenic patients on a psychological level as a disconnection between thoughts and actions, or as deficits of "willed intentions" (Frith and Done 1988), failure of inhibition (Spitzer et al 1994), inability to use context (Cohen and Servan-Schreiber 1992), a disruption of the reinforcement of adaptive behavior (Friston and Frith 1995), cognitive dysmetria (Andreasen et al 1996), executive dysfunction (Weinberger 1987), or deficient sensorimotor gating (Braff et al 1992). On a neural systems level, these dysfunctions have been associated with frontostriatal dysregulation (Robbins 1990), cortico-striato-pallido-thalamic (CSPT) dysfunction (Swerdlow and Koob 1987), and neural systems disconnectivity (Crow 1997; Hoffman 1997).

However, the "rules" underlying the cognitive disturbances of schizophrenia are still incompletely understood. While Bleuler's findings describe the cognitive, affective, and behavioral characteristics of schizophrenia, it has been difficult to quantify these disturbances experimentally.

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One aspect of this difficulty may have to do with the fact that many features of these disturbances are rooted in the temporal domain, i.e., how thinking, feeling, and acting change over time. In order to provide a conceptual and measurement framework for this temporal domain, we have begun to apply concepts and techniques from nonlinear dynamic systems analysis to determine how the behavior of schizophrenic patients is organized over time and how deficits in this organization can be related to the clinical, psychological, and neurobiological level of description of this illness (Paulus et al 1994, 1996).

A behavioral paradigm that enables the repeated measurement of many observations of behavior is key to examining the rules that determine how behavior changes over time. The two-choice guessing task has been used previously by several investigators to examine sequential patterns of behavior in schizophrenic patients (Frith and Done 1983; Lyon et al 1986). This task provides a versatile experimental probe to record relatively large numbers of behaviors from a limited set of behavioral alternatives. In this task, the subject is repeatedly asked to choose between two behaviors (i.e., a left or right key press) and is shown a stimulus on the computer screen that is random and noncontingent on the key press. Specifically, in our version of this task, a subject is asked repeatedly to "predict" whether a car will appear on the LEFT or RIGHT side of computer screen. There are several key concepts that have been explored with this task. First, Frith and Dolan (1996) have labeled as "willed intentions" a situation when subjects respond without being prompted to do so within a specific time frame. Second, decision making in the presence of an uncertain outcome has been proposed to involve a complex set of processes that comprise hypothesis testing, outcome evaluation, and strategy formation (Elliott and Dolan 1998). Third, the temporal architecture of the behavior exhibited on this task has been described as highly organized and nonrandom by several investigators (Lyon et al 1994).

We used the two-choice guessing task to clarify two basic questions about how behavior changes over time. First, how is the current behavior (LEFT/RIGHT key press) linked to previous behavior? Second, how is the current behavior linked to the previous LEFT/RIGHT presentation of the car, i.e., how does the preceding outcome of the "prediction" affect the current choice? The answer to these questions are key to understand the dynamic characteristic of behavior. It has been proposed that pathologic conditions are characterized by a maladaption of sequences of observations over time (Mandell 1983). Based on this notion, we propose that a disease model that attempts to explain the psychological dysfunctions in schizophrenic patients should be based on the notion of a distorted and dysreglated relationship between the past and the present behavior. More specifically, we hypothesize that one dysfunction in schizophrenia is characterized by the paradox of a simultaneous but oscillating increase and decrease in the dependency of the current behavior on the past behavior. This seemingly paradoxical change is can occur in a dynamic system that is in a state called intermittency (Manneville 1980). Intermittency occurs when a system is characterized by temporal bouts of highly regular or predictable sequences interspersed with episodes of highly irregular or unpredictable behavior. Intermittency is due to the transition between two different states of the system. First, a temporally stable, organizing rule exerts a strong influence on the behavior regardless of other intervening variables. Second, the system gradually escapes the influence of this organizing rule and exhibits a highly disorganized state until the system "is captured" again by the organizing influence of a temporally stable rule. On a neural systems level, this has been described in neural networks as parasitic attractors (Hoffman 1997), which lead to rigid and predictable sequences. The transition between the flexible adaptation of many different behavioral states to the demands of the current situation and intermittency has been proposed to be at the heart of a dynamic disease model (Manneville 1980), and has been supported by examining the temporal course of symptoms in schizophrenic patients (Duenki and Ambuehl 1996).

If the central hypothesis of characterizing schizophrenia by oscillating episodes of predictability and unpredictability is correct, several corollary statements can be examined. First, measures that quantify how behavior changes over time typically exhibit large fluctuations in intermittent systems (Ito and Gunji 1994). Second, average quantities frequently do not correspond to the most frequent observations, i.e., the mean value may correspond to a rare occurrence in the experiment. Third, the rule that underlies the temporal behavior of the system can be highly sensitive to experimental manipulations, reflecting the sensitivity of the system to even small perturbations. Fourth, temporal correlations between sequences may extend over a large temporal range. Consequently, in order to experimentally support these corollary changes, it is critical that a measure of fluctuation is used to describe the behavior of schizophrenic patients, to not rely on average measures, but to derive frequency histograms of subsequences with different dynamic properties, to vary systematically the experimental conditions that are used to collect the behavioral data, and to calculate the temporal relationships between behaviors over an extended period of time. Dynamic entropy quantifies the degree to which the past behavior predicts the current behavior. Measuring the range of entropy for different subsequences of choices quantifies the notion of behavioral dysregulation, which is based on the concept of oscillating fixed and random subsequences of behavior.

The central aim of this experiment was to examine the relationship between the dysregulation of sequential organization of behavior in schizophrenic patients and the demographic, clinical, neuropsychological, and psychological characteristics of these patients. Specifically, the following hypotheses were addressed. First, if pervasive behavioral dysregulation represents a complex process that reflects a fundamental property of the sequences of choices, then this behavioral dysregulation should be independent of short-term measures that are based on one or two consecutive choices. Second, if the dysregulation in sequential organization represents a fundamental enduring deficit of schizophrenic patients, then the degree of dysregulation should not be associated with relatively "peripheral" differing demographic characteristics of these patients. Third, if the dysregulation is associated with a fundamental cognitively mediated change in selection or sequencing of behavioral elements to form behavioral patterns, then the dysregulation should be related to the clinical assessment of the underlying organization of thinking or behavior. Fourth, if dysregulation of sequential organization is related to a disturbance of frontal functioning, then the degree of behavioral sequential dysregulation should be related to dysfunction on neuropsychological tests that have been shown to be dependent on the functioning of the prefrontal cortex.

In order to test these four hypotheses, choice task data of 500 LEFT/RIGHT responses from each of 30 schizophrenic patients were analyzed in a two-step process. First, a factor analysis determined whether the degree of dysregulation was independent of other choice task measures. Second, step-wise multiple regression analyses using demographic, clinical, neuropsychological, and psychological variables were computed to relate these variables to the degree of dysregulation and other choice task measures. Specifically, the Scale for the Assessment for Positive Symptoms (SAPS; Andreasen and Olsen 1982) and the Scale for the Assessment of Negative Symptoms (SANS; Andreasen 1982) were used to evaluate symptom levels, the Wisconsin Card Sorting Test (WCST; Heaton 1981) was used to evaluate executive functioning, and the Ego Impairment Index (Perry and Viglione 1992), derived from the Rorschach test (Exner and Weiner 1974) was used to assess disturbance in thought processing.

Methods and Materials

Subjects

A total of 30 schizophrenic patients (20 men and 10 women) ranging from 20 to 52 years of age (mean 36.3 years, SD 8.2), diagnosed according to DSM III-R criteria using a structured clinical interview (SCID-IP; Spitzer et al 1992) participated in this study. Of these patients, 23 were Caucasian, 4 African American, and 3 were Hispanic. The age of onset ranged from 10 to 35 years (mean 21.6 years, SD 6.7) and the duration of illness extended from 2 to 28 years (mean 14.6 years, SD 7.6). The number of hospitalizations ranged from 0 to 20 with a median of 4 hospitalizations. Finally, years of education varied from 6 to 18 years with a mean of 12.6 years (SD 2.5). Most of the patients received treatment while in this study and were treated with a mean chlorpromazine equivalent of 790 mg (SD 753) (Kessler and Waletzky 1981). The fluctuation spectrum analysis but not the current results for a part of this group of patients has been published elsewhere (Paulus et al 1996). Of the 30 patients, 2 patients had incomplete data sets from the Rorschach test, 5 had incomplete data sets on the WCST, and 1 patient did not complete the Choice Task.

Test and Procedures

The patients gave informed consent to be tested on the 128-card version of the Wisconsin Card Sorting Test (WCST; Heaton 1981) and the Rorschach test, administered and scored according to the Comprehensive System (Exner and Weiner 1974). The Ego Impairment Index (Perry et al 1992), EII, was derived from the Rorschach to measure disturbance in thought processes. Perry and co-workers (1992) found that in response to the unstructured and ambiguous blots, schizophrenic patients produce perceptually inaccurate and cognitively impaired responses. Several of the EII variables were selected for this study based on previous work indicating a high correlation of these variables with information processing measures in schizophrenia and schizotypal patients (Cadenhead et al 1993; Perry and Braff 1994; Perry et al 1992). These variables are R, the total number of responses given by the subject to ten stimuli; X−, a measure of perceptual accuracy; and Poor Human Experience Variable, which reflects disturbed thought processes and perceptual inaccurate responses in the context of human experiential percepts and is the single best predictor among these variables of disturbed thinking (Perry et al 1992). Finally, Derepressed Contents assesses the lack of ability to inhibit the expression of primitive content areas. In addition, various subscores of the Scale for the Assessment for Positive Symptoms, SAPS (Andreasen and Olsen 1982), and Scale for the Assessment of Negative Symptoms, SANS (Andreasen 1982), were used to clarify the relationship between clinical symptoms and the measures of behavioral organization obtained from the choice task behavior.

The two-choice guessing task paradigm has been described in detail elsewhere (Paulus et al 1994; 1996). Briefly, the following paradigm was presented on the computer screen: a house was displayed in the center flanked on either side by a sidewalk and a ditch as well as a road on the far left and right. The subject was told that in the house are several people waiting to catch a ride with a car that will come by on the left or right road. Only two people can wait at a time, one on each side, but neither can cross the ditch between the sidewalk and the road. The subject's task was to push the left or right button of a computer mouse in order to build a temporary bridge for one of the people, who may then cross the ditch to reach the car. A trial was initiated by the display of two people on the left and right sidewalk and terminated by showing the car for 250 msec after the subject had made his or her choice. The paradigm consisted of 500 presentations of the situation. For each trial, the subject's choice, the location of the stimulus on the screen, and the inter-trial interval was recorded.

Measures and Statistical Analyses

Three sets of measures were obtained from the sequences of choices: 1) the probability of LEFT versus RIGHT choice and the probability of SWITCH (i.e., LEFT followed by RIGHT or RIGHT followed by LEFT) was calculated to determine whether assessing simple response biases, which has been suggested by other investigators (Lyon et al 1986), could account for and be used instead of the more complicated dynamic measures; 2) the dynamic entropy was used to quantify the average degree to which the next choice can be predicted from the current choice (Paulus 1997; 1996, 1990). Moreover, to quantify the degree of fluctuation of this measure, the range of observed dynamic entropies was used to measure the degree of fluctuation of the predictability; and 3) mutual information measures were obtained (Herzel and Grosse 1995) to quantify the degree to which two or more observations share common information, i.e., are associated more frequently with each other than expected by chance. When calculating the mutual information between previous choice or previous external stimuli and the current choice, this measure can be used to determine the degree to which the external stimuli exert influence on the current choice. Moreover, by re-coding the two-choice data, e.g., a previous left-choice/left car (right-choice/right-car) and current left (right) choice is coded as 1 versus right (left) choice coded as 0, one can extract the degree to which a specific WIN-STAY/LOSE-SHIFT strategy (Evenden and Robbins 1984) was used more often than expected by chance. The concept of WIN-STAY/LOSE-SHIFT, i.e., the subject chooses the side where the stimulus was shown in the preceding trial, has been shown to be a critical determinant in animal paradigms of choice task behavior where random reinforcement contingencies were utilized (Evenden and Robbins 1984).

These choice task variables, shown in Table 1, were entered into a factor analysis using a eigenvalue = 1.0 criterion followed by a varimax rotation using the SPSS statistical package (Norusis 1990) to obtain linearly independent measures of the choice task behavior. In order to determine the relationship between sociodemographic, symptom, neuropsychological, and Rorschach measures and the choice task measures, a multiple regression analysis was chosen to determine the degree of shared variance determined hierarchically using a step-wise approach. Specifically, four sets of step-wise regression analyses were performed using SPSS statistical package (Norusis 1990). The dependent measures consisted of the factors retrieved by the factor analysis of the choice task variables. The threshold to enter the independent variable into the regression was set at $p < .05$; the threshold to remove an independent variable from the regression was set at $p > .1$.

Results

Factor Analysis

The factor analysis extracted three independent factors explaining 85.2% of measured variance of the entropy measures, the mutual information function measures, and the one-step probability measures. The correlation pattern following a varimax rotation is shown in Table 2. The correlation pattern with the factor solution indicates that the first factor results from using a WIN-STAY/LOSE-SHIFT strategy in the choice task. The second factor correlates strongly with the mutual information function and the situational mutual information function, indicating that this factor represents the degree to which the previous context influenced the current choice. The third factor correlates strongly with the metric entropy and the difference between the maximal and minimal entropy, quantifying the degree of dysregulation, i.e., the fluctuation between chaos and rigidity. In addition, this factor also correlates negatively with the switching probability and positively with the probability of chosing the left response. Thus, this factor corresponds to the dysregulation of responding on the choice task, which incorporates long

Table 1. The Average Choice Task Measures for 30 Schizophrenic Patients That Were Entered into the Factor Analysis

Choice task measures ($n = 30$)	Mean	Standard deviation	*t* Scores
Metric entropy	.65	.21	−2.8
$h_{diff} = h_{max} - h_{min}$	1.39	.59	−2.1
Mutual information	.10	.15	1.4
Cross mutual information	.02	.04	−3.3
Situational mutual information	.13	.15	−.7
Win stay/lose switch mutual information	.03	.04	−3.3
Switching probability	.40	.20	−.7
Left choice probability	.49	.15	.4
Win stay/lose switch probability	.55	.07	−3.8

T score differences are shown based on a 24 subject control group.

Table 2. The Correlation Patterns of the Rotated Factor Solution with the Original Variables; Correlations with $r < .30$ Are Omitted

Measures	WIN-STAY/ LOSE-SHIFT	Context	Dysregulation
Metric entropy	.35	−.56	−.66
$h_{diff} = h_{max} - h_{min}$	−.38	.50	.65
Mutual information	—	.95	—
Cross mutual information	.97	—	—
Situational mutual information	—	.95	—
Win stay/lose switch mutual information	.96	—	—
Switching probability	—	—	−.65
Left choice probability	—	—	.65
Win stay/lose switch probability	.95	—	—

Table 3. Symptomatic Assessment of Schizophrenia Patients Based on SAPS and SANS

SAPS and SANS global subscales ($n = 27$)	Mean	Standard deviation
Affective blunting	3.11	2.68
Alogia	2.14	1.26
Attention	2.00	1.47
Anhedonia	3.11	1.5
Avolition	3.85	1.20
Bizarre behavior	1.85	1.43
Formal thought disorder	2.85	1.68
Hallucinations	2.67	2.13
Delusions	3.67	1.39
Global SAPS	11.11	4.83
Global SANS	13.44	4.43

SAPS, Scale for the Assessment for Positive Symptoms; SANS, Scale for the Assessment for Negative Symptoms.

and repetitive runs of choices, predominantly on the left side. Based on this analysis, the behavior of schizophrenic patients on the choice task can be decomposed into three distinct factors. These factors consist of the degree of responding to the external stimulus based on a WIN-STAY/LOSE-SHIFT strategy, the degree of previous context influence on the current choice, and the degree of dysregulation incorporating long runs of left responses.

Relationship between WIN-STAY/LOSE-SHIFT, Context, or Dysregulation, and Sociodemographic Variables

The following sociodemographic and clinical variables were entered into three separate multiple regression analyses with the three factors, respectively: age, education, onset age, duration of illness, and chlorpromazine equivalent of current treatment. However, none of these variables entered into the regression analysis. Thus, none of these variables was able to predict the performance on the choice task.

Relationship between WIN-STAY/LOSE-SHIFT, Context, or Dysregulation, and Symptoms

Table 3 shows the average measures for the SAPS and SANS subscores for all patients with the complete set of measures which entered the step-wise regression analysis. None of the measures showed a significant correlation with any of the three factors. Thus, no regression analyses were generated, suggesting that the symptomatic status of the patients was not able to predict the performance on the choice task.

Relationship between WIN-STAY/LOSE-SHIFT, Context, or Dysregulation, and the WCST

None of the WCST measures (shown in Table 4) entered into a regression to predict the degree to which the patients used

Table 4. Average Measures for the WCST for All Patients with Complete Sets That Were Entered into the Stepwise Regression Analysis

Wisconsin Card Sorting Task measures (WCST) ($n = 25$)	Mean	Standard deviation
WCST categories	3.52	2.31
WCST errors	45.16	26.66
WCST perseverative errors	25.28	20.55
WCST perseverative responses	29.16	26.20

a win-stay/lose-switch strategy on the choice task. In addition no WCST measure was able to predict the degree to which the context was able to predict the next choice. However, two WCST measures, perseverative responses and categories achieved, entered into the regression analyses to predict the degree of dysregulation [$F(2,24) = 19.67$, $p < .01$]. Specifically, the more perseverative responses (standard coefficient = 1.1.0) and the more categories achieved (standard coefficient = .56), the higher the degree of dysregulation on the choice task. These two WCST measures accounted for 64% of the variance of the dysregulation factor.

Relationship between WIN-STAY/LOSE-SHIFT, Context, or Dysregulation, and Rorschach Variables

None of the EII variables (shown in Table 5) entered into the regression analyses to predict the degree to which context was used when choosing LEFT or RIGHT or the degree to which patients showed a dysregulation of choice sequences on the choice task. However, the Derepressed Content measure and Poor Human Experience Variable entered into a regression analyses to predict the degree to which the patients were using a WIN-STAY/LOSE-SHIFT strategy [$F(2,26) = 7.58$, $p < .01$]. Specifically, higher frequency of Derepressed Contents (standardized coefficient = .69) and lower Poor Human Experience Variable responses (standardized coefficient = −.56) predicted a higher degree of WIN-STAY/LOSE-SHIFT strategy on the choice task. These two Rorschach variables predicted 39% of the variance of the win-stay/lose-shift factor.

Table 5. Average Rorschach Candidate Variables for the Patients with Complete Data Sets

Rorschach measures ($n = 27$)	Mean	Standard deviation
Rorschach—R	17.18	5.47
Rorschach—Derepressed Contents	5.14	4.21
Rorschach—Poor Human Experience Variable	4.14	3.39
Rorschach—X−	5.92	4.53

Discussion

This investigation yielded four main results. In discussing these results, it is important to remember that in this task 1) the subject chooses LEFT or RIGHT by pressing the corresponding button; and then 2) the car appears randomly on the LEFT or RIGHT side of the computer screen. First, at least three independent dimensions determine the behavior of schizophrenic patients on the choice task. These independent dimensions are measured by: 1) the degree of WIN-STAY/LOSE-SHIFT, which is an indication that the patient is using a specific strategy in deciding LEFT versus RIGHT when the car randomly and noncontingently appeared on the LEFT or RIGHT side of the computer screen. For example, if the patients guessed LEFT "correctly" (the car was shown on the LEFT side after the key press), they would stay with the LEFT choice on the next trial. Conversely, if the patient guessed LEFT "incorrectly," they would shift to the opposite choice (RIGHT) on the next trial. 2) The degree to which the previous response strategy predicts the current choice. For example, when the patient used a STAY strategy and chose LEFT on the previous trial, then the patient is much more likely to choose LEFT again on the current trial independent of the subject's "correct" or "incorrect" prediction of the location of the car. 3) The degree of dysregulation on the choice task, which reflects the balance between fixed and random response sequences. For example, high levels of dysregulation occur when patients oscillated between bouts of highly perseverative choice sequences and highly unpredictable choice sequences. Second, demographic and clinical rating variables could not be used to predict any of these three dimensions. Third, in examining neuropsychological correlates of behavior the combination of an increased number of perseverative responses and an increased number of categories achieved on the WCST predicted an increase in the degree of dysregulation on the choice task. Fourth, in examining psychological correlates of behavior a lower frequency of Poor Human Experience Variable and a higher frequency of Derepressed Contents on the Rorschach predicted the degree to which patients used a WIN-STAY/LOSE-SHIFT strategy on the choice task. Each of these four areas will be examined in detail as follows.

First, the results of the factor analysis support the hypothesis that dysregulation of sequential organization, i.e., the increased fluctuation between highly predictable and highly unpredictable subsequences, is independent of any LEFT/RIGHT bias of responding and independent of the preceding choice. The analysis revealed that schizophrenic subjects employ several independent processes when choosing between the LEFT/RIGHT alternatives. These processes include 1) the selection of an outcome-dependent strategy; 2) the influence of the previous response strategy (context); and 3) the balance of fixed or chaotic choice sequences. As hypothesized, the schizophrenic deficit is temporally intermittent and can be quantified by considering the stability of behavioral strategies over time. The dysregulation of sequential organization, as measured by the range of local dynamic entropies, comprises an independent dimension of the behavior in this task. Specifically, if a subject is completely influenced by the previous LEFT/RIGHT presentation of the external stimulus, there should be no systematic relationship between individual choices, since the presentation of the stimulus is randomly generated. In contrast, if the subject's choices are completely independent of the presentation of the car stimulus, a highly nonrandom sequence may be generated by the subject's biases. The three factors reflect the competition of these processes on the current behavior. For example, a subject using a "pure" WIN-STAY/LOSE-SHIFT strategy for a number of trials on the task would generate a random sequence due to the random presentation of the stimuli. In contrast, a highly predictable and highly nonrandom sequence is generated if the subject changes to a strategy characterized by self-generated response repetition. The dysregulation factor quantifies the degree to which the subject switches between these different strategies over 500 trials in this task. A high degree of dysregulation indicates that few changes in strategy occur, resulting in a few highly unpredictable sequences representing the transition from one strategy to another and many highly predictable subsequences reflecting the repetitive application of the same strategy. This complex interaction of rules has been observed previously in this task by Lyon and co-workers (1994). Specifically, using a response time analysis, Lyon and colleagues suggested that schizophrenic patients generate increased different patterns and exhibit a higher degree of variability on the choice task. These authors interpreted these findings within the framework of increased stimulation, which induces new responses, and suggest that the complexity of the behavior of schizophrenic patients is a result of the inability of normal behavior to occur in competition with dopaminergically driven stereotypically emitted sequences. We would like to extend this hypothesis to include recent conceptualizations of the schizophrenic deficit as resulting from "disconnected" neural networks (Cohen and Servan-Schreiber 1992; Hoffman 1997). Specifically, dopaminergic innervation critically affects both cortical and subcortical circuits (Weinberger 1987) that are thought to be involved in the initiation, competition, and maintenance of behavioral responses (Lyon and Robbins 1975). Based on information processing paradigms, a fundamental disruption of these reverberating circuits has been proposed as a central focus of the schizophrenic dysfunction (Swerdlow and Koob 1987). Here, we propose that this neural circuit dysfunction is not fixed over time but is temporally intermittent and results in an alternating increase of both fixed and chaotic response sequences in a single test session.

Second, the results support the hypothesis that schizophrenic patients' abnormally increased degree of dysregulation is not related to specific demographic characteristics. The finding that none of the symptom scales significantly predicted the response characteristics on the choice task did not support the hypothesis that patients with more symptoms along the disorganized spectrum, e.g., formal thought disorder, would exhibit an increase in dysregulated responding on the choice task. Symptoms of schizophrenia undergo significant temporal fluctuation while cognitive dysfunctions are more persistent. Therefore, the lack of correlations may be due to unstable symptom patterns during the test session. Both medication and duration of illness were not controlled for in this investigation and may contribute to the lack of symptomatic correlations. The most likely interpretation is that strategies of prediction and dysregulation are more related to the "core" cognitive deficits of schizophrenia (linked to Bleuler's primary symptoms), and less related to more transient shifts in positive and negative symptoms (linked to Bleuler's secondary symptoms).

Third, the number of perseverative responses and categories completed on the WCST predicted the degree of dysregulation on the choice task. This result supports the hypothesis that executive functioning, as measured by the WCST, is related, albeit in a complex manner, to sequential organization as measured by the fluctuations of predictability in the choice task. Perseveration and categories measures reflect two seemingly opposite processes that are often negatively correlated. Examining the correlation patterns with the degree of dysregulation revealed that the WCST measures of impaired executive functioning (e.g., perseverative responses) correlated negatively with the minimal entropy. Thus, patients with more perseverative responses generated a more predictable subsequence in the two choice guessing task. In contrast, the categories measure correlated negatively with the maximal entropy: patients with more categories achieved generated a fewer highly unpredictable sequences on the choice task. Examining the composition of the overall sequence characteristics in the choice task may help to better understand this counterintuitive relationship. As shown in Figure 1, the choice task can include subsequences of different degrees of predictability, such that highly unpredictable sequences can be associated with new behavioral strategies. The degree of dysregulation may represent an imbalance between initiation of novel behaviors (high entropy sequences) and the maintenance of ongoing predictable behaviors (low entropy sequences). As presented in Figure 1C, there is a striking nonuniform transition between low-entropy sequences and increased high-entropy sequences. Schizophrenic patients appear to be stuck in a strategy that comprises the bifurcation of two opposite cognitive states, i.e., that of high repetition and low uncertainty and that of low repetition and high uncertainty. This may be a novel and quantitative approach of measuring ambivalence, a core Bleularian feature of schizophrenia. Other investigators have proposed that difficulty initiating action is one component of the psychological dysfunction in schizophrenia (Frith and Done 1988), which may lead to perseverative behavior (Crider 1997). Perseverations and related ambivalence have been linked to dysfunction in prefrontal activation of new action and impaired basal ganglia competition of alternate behavioral programs (Robbins 1990).

Fourth, the relationship between the Rorschach-derived measures of cognitive processing and choice task behavior is of interest. Specifically, the frequent use of a WIN-STAY/LOSE-SHIFT strategy was predicted by a low score on the Poor Human Experience Variable. This variable measures the degree of disturbed thought processes or perceptual inaccuracies and has been linked to thought disturbance in schizophrenic patients (Perry and Braff 1994; Perry et al 1992). It appears that patients with relatively intact thought and perceptual processes use a choice strategy that relies on the accurate perception and processing of the subject's experience of the previous situation, i.e., the LEFT/RIGHT choice followed by the presentation of the car on the LEFT/RIGHT side. Thus, the relationship of thought disturbance and the use of an outcome-dependent strategy supports the relationship between cognitive organization and sequential organization in the choice task. The direct relationship between inhibitory failures as measured by the Derepressed Contents variable and the win-stay/lose-shift strategy may represent a separate process that leads to a similar strategy. Specifically, a lack of inhibition may lead to an immediate or even impulsive pattern of responding on the choice task by associating the previous situation with the current response. Thus, two separate and conceptually different processes may lead to similar behavioral patterns. This two-process hypothesis could be tested in a larger patient cohort by examining the variability of inter-response intervals. We would expect that a more impulsive pattern of responding is associated with a shorter inter-response interval than the more evaluative approach such as the WIN-STAY/LOSE-SHIFT strategy.

To summarize, three of the four hypotheses were supported: 1) behavioral dysregulation is independent of short-term measures that are based on one or two consec-

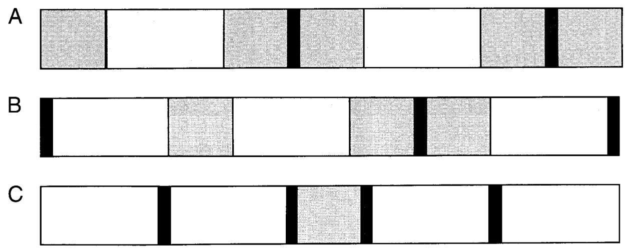

Figure 1. This figure shows schematically different degrees of dysregulation of sequential organization. The different gray-shaded blocks correspond to subsequences with different degrees of predictability. Dark gray blocks represent highly unpredictable subsequences, mid-gray blocks correspond to moderately unpredictable subsequences, and light-gray blocks refer to highly predictable subsequences. The bars represent a fixed number of choice task trials. The first bar **(A)** consists of five moderately unpredictable sequences, two highly predictable, and two highly unpredictable subsequences. In this example, highly predictable and high unpredictable subsequences occur less frequently than moderately unpredictable subsequences, indicating a low degree of dysregulation. The second bar **(B)** consists of three highly predictable, moderately unpredictable, and highly unpredictable subsequences indicating an equal distribution of different entropic subsequences and a moderate degree of dysregulation. The third bar **(C)** consists of four highly predictable and highly unpredictable subsequences and one moderately unpredictable subsequence. In this example, the increased frequency of subsequences with either low or high entropy indicates a high degree of dysregulation.

utive choices; 2) the degree of dysregulation is not associated with relatively "peripheral" differing demographic characteristics of schizophrenic patients; and 3) the degree of behavioral sequential dysregulation is related to neuropsychological tests that have been shown to be dependent on the functioning of the prefrontal cortex. However, the degree of dysregulation was not related to the clinical assessment of the underlying organization of thinking or behavior. These results support the notion that the intermittent disruption of sequential organization in schizophrenic patients is best captured by approaches that explicitly assess the temporal domain of behavior. This temporal domain includes sequencing and timing of behavior that we label "temporal architecture." Many investigators have highlighted the enormous variability of measurement results of schizophrenic patients. Future investigations will need to determine whether this dysfunction of the temporal architecture of behavior in schizophrenic patients can be replicated in other paradigms and can be linked to a characteristic disruption of neural systems.

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