



Behavioural dysregulation of decision-making in deficit but not nondeficit schizophrenia patients

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Abstract

This study aimed to determine whether deficit but not nondeficit schizophrenia showed dysregulation of decision-making. In a two-choice prediction task, the subject is asked to predict whether a stimulus appears on the left or right side of a computer screen. Schizophrenia patients were divided into 12 patients with and 12 patients without deficit syndrome and compared to 12 healthy control subjects. Dynamical entropy and mutual information analyses were used to determine underlying strategies and the degree to which sequences of responses are nonrandom. When compared to controls, deficit but not nondeficit schizophrenia patients showed a dysregulation of decision-making characterized by an increased oscillation between highly predictable and highly unpredictable response sequences. Moreover, in deficit patients, the previous choice was more predictive of the current response. Therefore, the two-choice prediction task may be useful in differentiating between deficit and nondeficit schizophrenia.

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1. Introduction

Decision-making is an important but complex process in everyday life. In general, decision-making occurs whenever a person has an option to select among several available alternatives that can be associated with positive or negative outcomes, which may be uncertain. The two-choice prediction task is a simple behavioural paradigm to probe how subjects select between different

response alternatives and how they adjust their decisions based on the history of correct and incorrect decisions. The fact that the reinforcement is random but nontransparent to the subject enables us to better control the reinforcement history and allows us to examine the degree to which fluctuations in the past, correct vs. incorrect predictions, influence decision-making. Although there are many other decision-making situations, the two-choice task probes some of the most fundamental processes (feedback, reward/punishment effects) associated with decision-making. Using this task, previous investigations have shown that schizo-

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phrenia patients exhibit a profound dysregulation of decision-making. Within the same test session, schizophrenia patients oscillate between highly predictable and highly unpredictable response sequences (Paulus et al., 1994, 1996, 1999). This pattern of responses supports the general notion that decision-making in schizophrenia patients is based on intermittent fluctuation between rigid and predictable and highly erratic rules. This view is consistent with the general hypothesis that the cognitive dysfunction underlying schizophrenia is not appropriately described as an increase or decrease in decision-making capacity but is more consistent with the hypothesis of a dysregulated cognitive substrate. Other investigators have proposed similar concepts in both the temporal domain of cognition, e.g. as cognitive dysmetria (Andreasen, 1999), or in the spatial domain of neural systems functioning, e.g. the disconnectivity of neural systems (Friston et al., 1995).

One aspect of the complexity of the schizophrenia phenotype is the fact that it is extremely heterogeneous (Fenton et al., 1997). This heterogeneity has led a number of investigators to divide the disorder into subtypes based on clinical psychopathology and course of illness (Fenton et al., 1997; Arndt et al., 1991; Peralta et al., 1992; Arango et al., 2000). In particular, the distinction between deficit and nondeficit subtypes has received both clinical and research interest. Initially, this distinction was conceptualised by Carpenter et al. (1988), who differentiated a subgroup with profound and long-term negative symptoms combined with the inability to function independently in society. These patients were characterized as suffering from deficit-syndrome schizophrenia. In comparison, those patients who did not show these symptoms and associated impairments were called nondeficit-syndrome schizophrenia patients. Thus, the deficit-syndrome in schizophrenia defines a subtype with enduring, idiopathic negative symptoms (Kirkpatrick et al., 1989). A 15-year longitudinal follow-up study revealed that nearly one third of patients developed a deficit syndrome (Bottlender et al., 1999). In subsequent studies, this conceptualisation has been further validated. Initially, it was found that neurological signs were associated with the presence of the deficit syn-

drome (Buchanan et al., 1990). Other studies have shown impaired cognitive performances in deficit vs. nondeficit schizophrenia patients (Buchanan et al., 1990; Bustillo et al., 1997; Buchanan et al., 1997). Moreover, recent functional neuroimaging investigations support the notion that deficit but not nondeficit schizophrenia patients exhibit prefrontal hypoactivity during memory retrieval (Heckers et al., 1999). Finally, a study with proton magnetic resonance spectroscopy for the left and right medial prefrontal cortex was performed in schizophrenic patients with deficit and nondeficit syndrome and healthy control subjects. Lower ratios of *N*-acetylaspartate to creatine plus phosphocreatine suggest a neuronal dysfunction in the frontal region of deficit but not nondeficit patients (Delamillieure et al., 2000).

If deficit-syndrome schizophrenia patients show profound cognitive dysfunction that involves the prefrontal cortex, and if decision-making is critically dependent on intact functioning of this system (Paulus et al., 2001), it was hypothesized that the previously observed dysregulation of decision-making is exaggerated in deficit relative to nondeficit-syndrome schizophrenia patients. Support for this hypothesis would help to validate the distinction between deficit and nondeficit schizophrenia patients. In addition, it would provide an important dimension to separate patient groups to examine the neural substrate underlying the decision-making dysfunctions in these patients. Finally, differential decision-making dysfunctions may be used as a phenotypic marker to predict long-term outcome as measured by deficit vs. nondeficit status.

To test this hypothesis, schizophrenia patients were recruited from a hospital that provides both short-term and long-term facilities for patients to obtain similar sample sizes of deficit and nondeficit patients according to the Schedule for the Deficit Syndrome (Kirkpatrick et al., 1989). The response sequences generated by the schizophrenia patients were analysed using nonlinear dynamical system techniques (Paulus et al., 1997) to determine the degree to which the previous response predicted the current response, whether the previous stimulus predicted the current response, and whether the current sequence of responses was

part of a highly predictable or highly unpredictable set of response sequences. These techniques enable one to obtain measures of how behaviour is organized over time and, therefore, can be used to address the question of the disruption of the temporal architecture of behaviour in schizophrenia. In addition, we examined the dynamical characteristics of the response sequences generated by both patients and controls during three different reinforcement conditions in order to determine whether the dysregulation of decision-making was sensitive to the degree to which a subject chose a 'correct' response.

2. Methods

2.1. Participants

The experiment was approved by the Ethics Committee of the Psychiatric Services of Aargau Canton and the Ethics Committee of the Psychiatric University Hospital Zurich. Fifty-four patients with schizophrenia and 39 controls were tested. The patients were diagnosed according to ICD-10 and DSM-IV diagnostic criteria based on an individual semi-structured psychiatric interview by an experienced clinician using the German version of the International Diagnostic Checklist (Hiller et al., 1996). Additional information was available from the treating psychiatrist and hospital chart documents. Forty-three patients were recruited through the Inpatient Psychiatric Services of Aargau Canton 'Klinik Königsfelden' (Switzerland). The hospital comprises three facilities: a short-term facility (mean duration of stay \approx 3–4 weeks for acute psychiatric crises), a long-term facility, and a geriatric facility (patients > 65 years). Most of the long-term facility patients are schizophrenic, are not able to live without professional psychiatric help, and may remain in the facility for many years; after long-term rehabilitation, some of them are able to live in homes. Eleven patients were recruited through the Psychiatric University Hospital 'Burghölzli' (sector ost) in Zurich (Switzerland), which also comprises a long-term and a short-term facility. For this study, we recruited patients from both the short-term and the long-term facilities of these two psychiatric hospitals.

The schizophrenia patients included 42 men and 12 women, with a mean age of 37.7 years (S.D. 11.4) and a mean duration of illness of 13.2 years (S.D. 11.1). Controls (mean age: 37.1, S.D. 14.1) were hospital employees or were recruited through local advertisements. The comparison group included 23 men and 16 women. A semi-structured interview in the healthy comparison group revealed no personal history of psychiatric disorder, substance abuse, or major medical disorder and established absence of psychosis in first-degree relatives.

The deficit and nondeficit schizophrenia patients were different in relation to age and gender [deficit schizophrenia: mean age (S.D.): 42.9 (10.0), gender: 24 males, 9 females; nondeficit schizophrenia: mean age (S.D.): 29.5 (8.3), gender: 18 males, 3 females]. Age- and gender-matched subgroups were used to compare the differences among deficit schizophrenia, nondeficit schizophrenia and controls. Demographic data and relevant clinical characteristics are presented in Table 1.

2.2. Psychometric scales

Symptoms were rated with the Positive and Negative Syndrome Scale (Kay et al., 1987). Thirty-three of the 54 patients with schizophrenia were classified as having deficit-syndrome schizophrenia and 21 were classified as having nondeficit-syndrome schizophrenia using the Schedule for the Deficit Syndrome by an experienced clinician (Kirkpatrick et al., 1989).

2.3. Procedure of the choice task

The purpose of this task is to quantify decision-making characteristics by examining the sequential patterns of responses, which are based on repeated selection between action alternatives with an uncertain outcome. Each subject was given instructions on the computer screen. Briefly, a house is shown in the centre of the computer screen with a person on the left and the right side. The subject is told that a car will appear on the left or the right side. The task for the subject is to predict where the car will appear. The subject is told that the car will appear briefly (250 ms) *after* a

Table 1

Demographic data and relevant clinical characteristics of control subjects and patients with deficit and nondeficit forms of schizophrenia

		Deficit schizophrenia N=12	Nondeficit schizophrenia N=12	Controls N=12
Age	Mean (S.D.)	35.0 (7.2)	33.7 (8.5)	33.9 (8.3)
Gender	Men	10	10	10
	Women	2	2	2
Duration of illness	Mean (S.D.), in years	12.4 (8.7)	5.3 (4.6)	
Medication	Typical antipsychotics	7	3	
	Atypical antipsychotics	4	7	
	Typical+ atypical antipsychotics	1	1	
	Unmedicated	0	1	
PANSS	Positive symptoms	17.8 (5.3)	16.7 (7.8)	
	Negative symptoms	19.7 (3.8)	15.7 (4.6)	
	General psychopathology	42.8 (6.5)	37.0 (9.5)	
	Depression	10.3 (4.8)	9.0 (4.1)	

response has been made. The subject uses a left or right mouse button to decide where he/she thinks the car will come. The subject can use either the right or the left hand. A new trial begins immediately after the display of the car. The subject is not given any information about the sequence of stimulus presentations. The two-choice prediction task consists of three sets of trials. For the first 128 trials, the presentation of the car is based on the subject's response and the subject 'correctly' predicts the location of the car in 64 trials. For the next 64 trials, the subject 'correctly' predicts in 13 trials. Finally, for the next 64 trials, the subject 'correctly' predicts in 51 trials. Thus, the reinforcement probability is 50% during the first set of trials, approximately 20% during the second set, and approximately 80% during the third set of trials. The basic measures consist of the subject's response, the presentation of the car, and the latency to select a response, i.e. the time from the beginning of the trial to the button press.

2.4. Nonlinear analysis

The nonlinear analysis of sequences of responses on the two-choice prediction task enables one to quantify the degree to which external

stimuli, previous behaviour, and long-range strategies influence decision-making and whether the behavioural disturbance in schizophrenia may be due to an altered temporal pattern of these influences. Three sets of measures were obtained from the sequences of responses to assess whether (1) subjects exhibit response biases; (2) the current response can be predicted by the previous response, the previous presentation of the stimulus, or the previous outcome of the prediction; (3) the current response was part of a highly predictable or highly unpredictable response sequence. First, response bias measures were obtained to determine whether subjects were more likely to select *right* vs. *left* or were more likely to *switch* between responses than to *stay* with the same response. Second, the mutual information function was used to determine the degree of nonrandomness between two observations. Mutual information functions (Herzel and Grosse, 1995) are based on the logarithmic likelihood ratio between the observed frequency of an event and the expected frequency of an event. These functions quantify the degree to which the co-occurrence of two observations is above chance level in units of bits. For example, if the subject selects the *left* response more often when the car has been shown previously on the left side, the mutual information will quantify the

bits of information contained in the response selection due to knowing the previous location of the car. Specifically, the sequence of responses and the sequence of stimulus presentations are coded so as to examine the relationship between the current response and the previous response (*left* or *right*), the current response and the previous stimulus (car on the *right* or *left*), and the current response and the previous outcome ('correct' prediction or 'incorrect' prediction). Third, the dynamical entropy was computed for sequences of responses to quantify the degree of response sequence uncertainty. These behavioural analyses were based on techniques that have been developed in the context of nonlinear dynamical systems (Eckmann and Ruelle, 1985), complex physical systems (Haken, 1996), and statistical mechanics of physical (Fujisaka and Inoue, 1990) and dynamical systems (Ruelle, 1978). The degree of dysregulation was defined by the range of subsequent entropies, i.e. $h_{\text{diff}} = h_{\text{max}} - h_{\text{min}}$. A small number signifies that most response sub-sequences are similarly predictable. In contrast, a large number indicates that some response sub-sequences are highly predictable and other response sub-sequences are highly unpredictable during the same test session. This measure quantifies the degree to which divergent sequential strategies are used during this task. For example, a high degree of dysregulation supports the hypothesis of an intermittent process that leads to both highly predictable sequences as well as highly unpredictable sequences of decisions.

2.5. Statistics

All statistical analyses were performed using STATISTICA/w™ (STATSOFT™) and SPSS for Windows (9.0.0). For the statistical analyses, a repeated measures analyses of variance (ANOVA) with subject group as a between- and reinforcement-condition as a within-factor was used. First, to replicate previous findings in dysregulation, metric entropy, and mutual information, measures were compared between schizophrenia patients and control subjects. Second, schizophrenia patients were divided into a group with deficit syndrome vs. a group with nondeficit syndrome. The entropy and

mutual information measures for the deficit- and nondeficit-schizophrenia patients were compared to the results obtained from control subjects. Third, in the schizophrenia group, Spearman rank correlation between choice measures and clinical symptoms were calculated.

2.6. Key measures for the two-choice prediction task

2.6.1. Metric entropy

Entropy measures the 'sequential order' within sequences of responses. Low entropy means that the sequences of responses is highly predictable; high entropy implies that the response sequences are highly unpredictable. Thus, predictability is a collateral measure for the degree to which sequences of responses are based on a consistent internal strategy. However, this measure does not take into account the dependency of the response sequence on external stimuli, which is measured by the cross-mutual information (see below).

2.6.2. Dysregulation

Dysregulation quantifies the range of sequence entropies found during the course of an experiment. A high value of dysregulation indicates that the response sequences that occurred during the experiment are characterized by both 'perseverative tendencies' and highly unpredictable or dynamically 'chaotic' strategies.

2.6.3. Entropy distribution

Entropy distribution indicates whether the response sequences generated by the subject were entropically homogenous, i.e. showed a similar level of unpredictability, or were dynamically heterogeneous, i.e. response sequences that were either highly predictable or highly unpredictable.

2.6.4. Mutual information

The mutual information quantifies the degree to which the previous response predicted the current response and provides a measure of the immediate influence of the past response on the decision in the current trial.

Table 2
Mean values and S.D. (in parentheses) of significant data

Measure	Schizophrenia (N=54)	Controls (N=39)
Dysregulation (%)		
50/50	0.99 (0.3)	0.93 (0.20)
20/80	1.09 (0.44)	0.91 (0.24)
80/20	1.27 (0.42)	1.22 (0.36)
Metric entropy (%)		
50/50	0.78 (0.10)	0.81 (0.05)
20/80	0.76 (0.10)	0.78 (0.06)
80/20	0.64 (0.14)	0.69 (0.11)
Mutual information (%)		
50/50	0.05 (0.09)	0.02 (0.03)
20/80	0.07 (0.12)	0.04 (0.05)
80/20	0.16 (0.20)	0.10 (0.11)

Measure	Deficit schizophrenia (N=12)	Nondeficit schizophrenia (N=12)	Controls (N=12)
Dysregulation (%)			
50/50	1.12 (0.31)	0.91 (0.16)	0.89 (0.20)
20/80	1.22 (0.72)	0.88 (0.27)	0.92 (0.31)
80/20	1.33 (0.39)	1.36 (0.46)	1.17 (0.39)
Metric entropy (%)			
50/50	0.72 (0.12)	0.79 (0.08)	0.81 (0.07)
20/80	0.73 (0.10)	0.80 (0.06)	0.78 (0.07)
80/20	0.59 (0.15)	0.64 (0.14)	0.69 (0.08)
Mutual information (%)			
50/50	0.09 (0.11)	0.02 (0.04)	0.03 (0.04)
20/80	0.12 (0.13)	0.02 (0.02)	0.05 (0.06)
80/20	0.20 (0.20)	0.14 (0.16)	0.08 (0.11)

2.6.5. Cross-mutual information

The cross-mutual information quantifies the degree to which the previous location of the stimulus (presentation of the car on the *left* or *right* side) is able to predict the current response. As opposed to entropy and mutual information, this measure quantifies the influence of external stimuli on the sequences of responses.

2.6.6. Win-stay/lose-shift

The most commonly observed strategy used by subjects on this task is win-stay/lose-shift, i.e. select the same response if it correctly predicted the location of the car, shift otherwise.

3. Results

Mean values and S.D. of statistically significant measures are presented in Table 2.

3.1. Comparison between schizophrenia (deficit and nondeficit patients N=54) vs. controls (N=39)

3.1.1. Dysregulation

Schizophrenia patients relative to controls exhibited significantly more dysregulated behaviour ($F=5.2$, d.f. = 1, 87, $P<0.03$). This effect was independent of the reinforcement conditions.

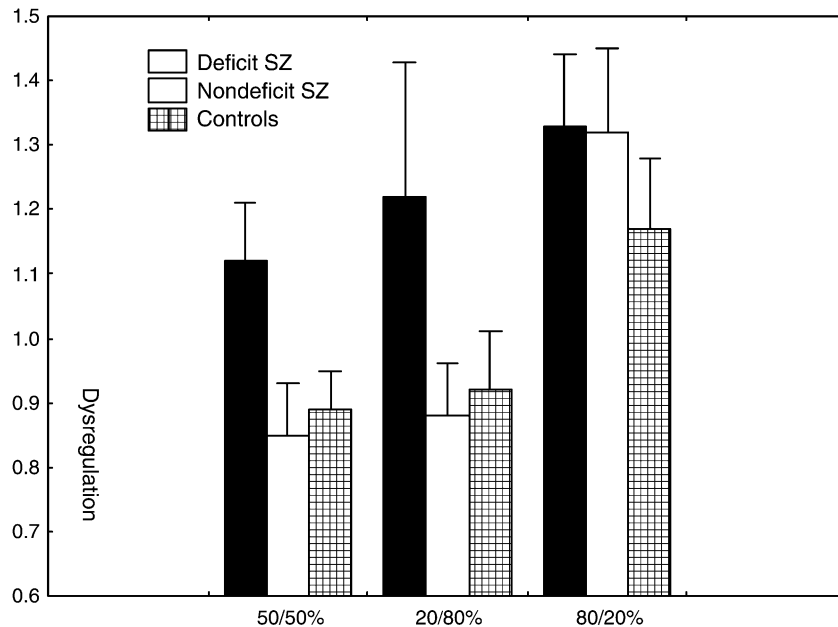


Fig. 1. Schizophrenia patients with the deficit syndrome exhibited significantly more dysregulation (max.-min. entropy) in conditions 1 (50/50) and 2 (20/80) than controls and schizophrenia patients with the nondeficit syndrome.

3.1.2. Metric entropy

The sequences of responses generated by schizophrenia patients were more predictable than those of controls and, therefore, characterized by a lower metric entropy (main effect: $F=5.7$, d.f. = 1, 87, $P<0.02$). This effect was independent of the reinforcement condition.

3.1.3. Mutual information

The previous response tended to better predict the current response in schizophrenia patients relative to controls as indicated by higher mutual information ($F=3.9$, d.f. = 1, 87, $P=0.052$). This effect was independent of the reinforcement condition.

3.2. Comparison of deficit schizophrenia ($N=12$) vs. nondeficit schizophrenia ($N=12$) vs. controls ($N=12$)

3.2.1. Demographics

Demographic data of control subjects and of schizophrenia patients with and without the deficit syndrome are presented in Table 1. The groups

were similar in age and gender. The duration of illness was higher in the deficit group, indicating that the deficit patients had an earlier onset of illness than the nondeficit group. Nondeficit patients preferentially received atypical antipsychotics, whereas most of the deficit patients were treated with typical antipsychotics.

3.2.2. Dysregulation (Fig. 1)

The degree of dysregulation differed significantly across the three groups ($F=3.7$, d.f. = 2, 32, $P<0.04$). Reinforcement probability significantly affected the degree of dysregulation in all groups. Specifically, the intermittent fluctuation between highly predictable and highly unpredictable response sequences was more pronounced during the 80% reinforcement condition than during the 20 or 50% reinforcement condition. The reinforcement conditions, however, did not differentially affect the groups (interaction: $F=0.6$, d.f. = 4, 64, n.s.). The post hoc test shows significant differences between deficit syndrome patients and controls in condition 1 (50/50%; $F=4.5$, d.f. = 1, 32, $P<0.02$), and between nondeficit syndrome

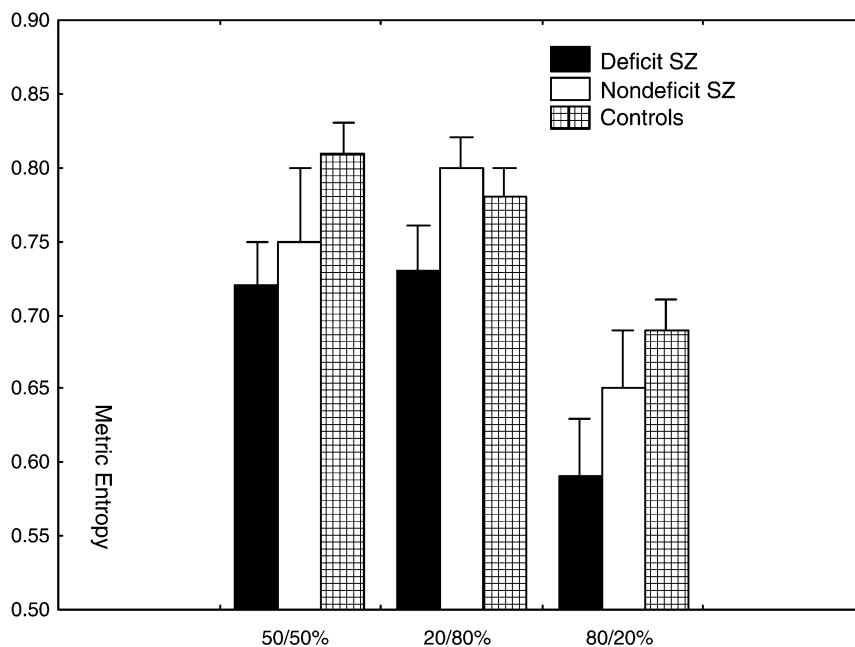


Fig. 2. Metric entropy in schizophrenia patients with the deficit syndrome was less than in healthy controls (conditions 1–3: 50/50, 20/80, 80/20) and schizophrenia patients with the nondeficit syndrome (conditions 1 and 2: 50/50, 20/80).

and deficit syndrome patients in condition 1 ($F=4.0$, $d.f.=1, 32$, $P<0.04$), but no differences between nondeficit patients and controls. There were no differences in conditions 2 (20% correct predictions) and 3 (80% correct predictions).

3.2.3. Metric entropy (Fig. 2)

The response sequences generated by schizophrenia patients with the deficit syndrome were significantly more predictable than those generated by controls and nondeficit schizophrenia patients (mean: $F=5.0$, $d.f.=2, 32$, $P<0.01$). The average predictability of the responses for the different reinforcement conditions was not differentially affected across patients or controls (interaction: $F=0.5$, $d.f.=4, 64$, $n.s.$) with less metric entropy in condition 3 (80/20%). In post hoc tests, the differences between deficit syndrome and comparison subjects were significant in condition 1 (50/50%, $F=5.8$, $d.f.=1, 32$, $P<0.02$) and showed a tendency to differ in condition 3 (50/50%, $F=3.7$, $d.f.=1, 32$, $P<0.06$). Patients with the deficit syndrome and with the nondeficit syndrome dif-

fered significant in conditions 1 ($F=3.7$, $d.f.=1, 32$, $P<0.06$) and 2 ($F=4.5$, $d.f.=1, 32$, $P<0.04$). There were no differences between nondeficit syndrome and comparison subjects.

3.2.4. Entropy distribution

The distribution of response sequences characterized by different degrees of predictability as measured by the dynamical entropy differed significantly across groups (Fig. 3a). A Cohen's d effect size analysis revealed that the effect size difference was large for the frequency of highly predictable (low entropy) and highly unpredictable (high entropy) response sequences between deficit schizophrenia patients and controls (Fig. 3b). Although there was some indication of increased dysregulation in nondeficit schizophrenia patients [$d_{\max}(\text{low entropy}) \approx 0.5$; $d_{\max}(\text{high entropy}) \approx 0.25$], this effect was significantly smaller than that in deficit schizophrenia patients [$d_{\max}(\text{low entropy}) \approx 1.0$; $d_{\max}(\text{high entropy}) \approx 0.90$].

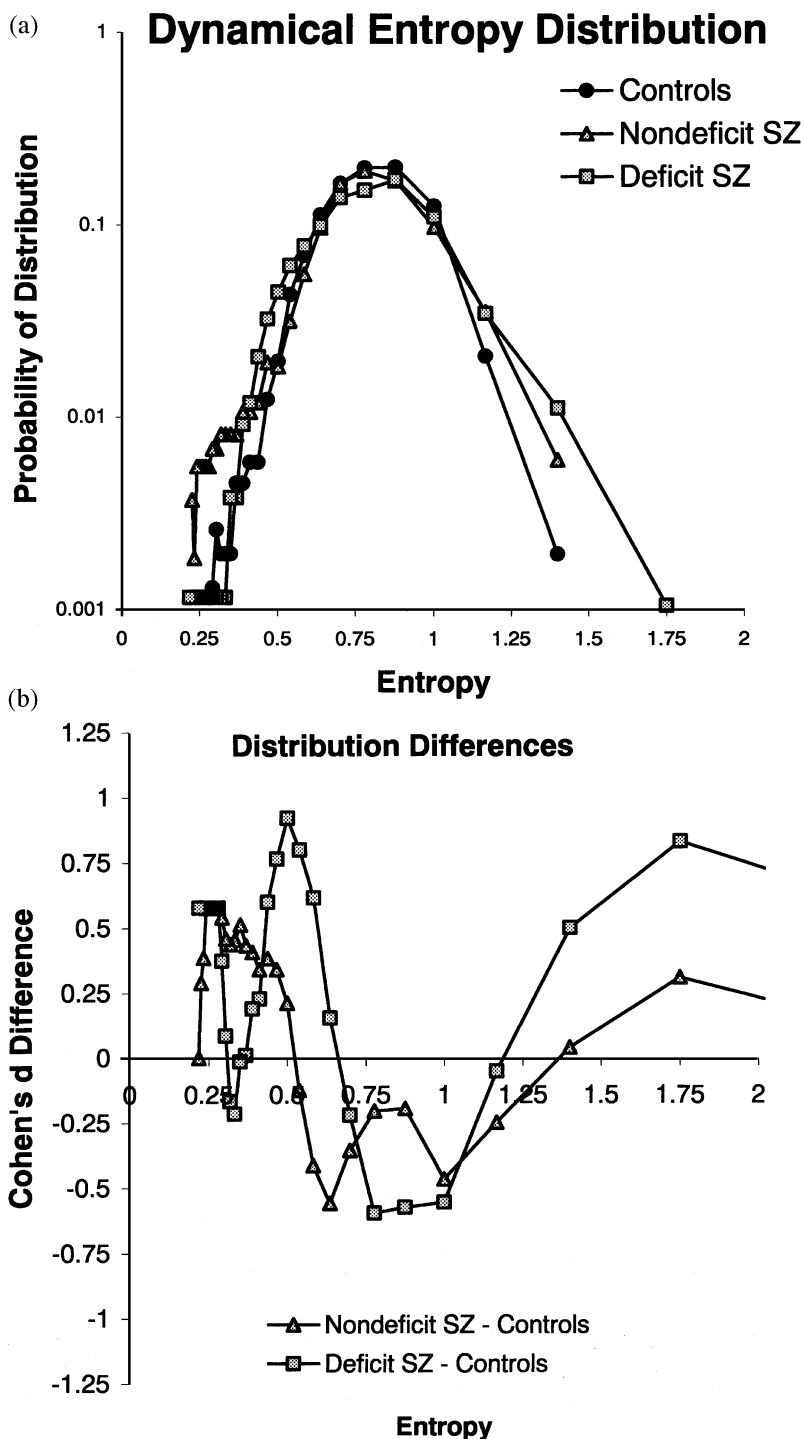


Fig. 3. (a) The entropy distribution for the control group, the deficit schizophrenia patients and the nondeficit schizophrenia patients. (b) The effect size of the difference between the deficit schizophrenia patients and the control group. The entropy distribution supports the hypothesis that deficit schizophrenia patients but not nondeficit schizophrenia patients show more highly predictable (low entropy) and highly unpredictable (high entropy) response sequences.

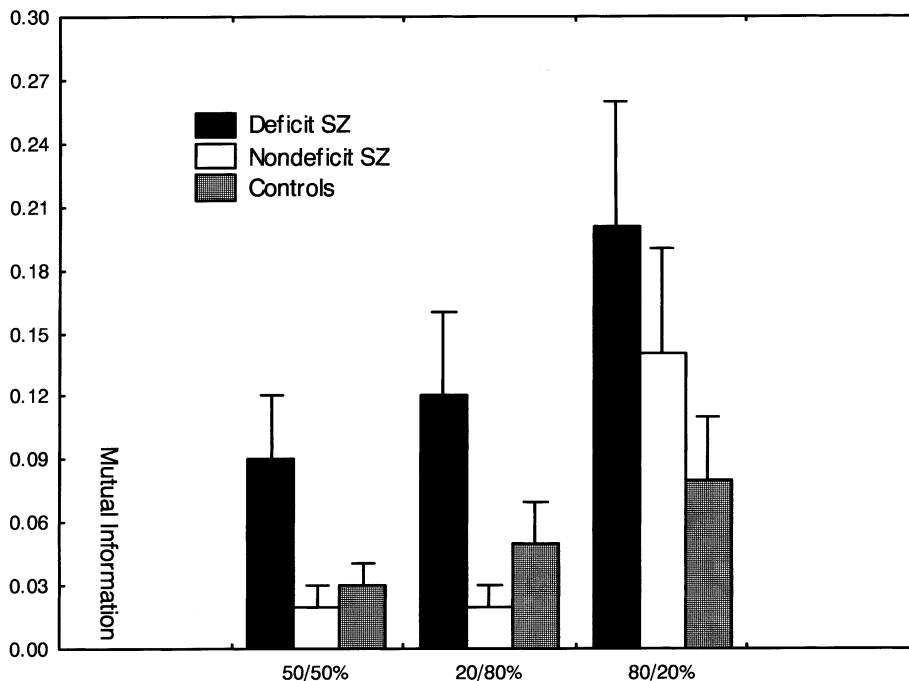


Fig. 4. Schizophrenia with the deficit syndrome showed higher mutual information in conditions 1–3 (50/50, 20/80, 80/20) than controls and schizophrenia with the nondeficit syndrome.

3.2.5. Mutual information (Fig. 4)

The degree to which the previous response predicted the current response differed significantly across groups and across reinforcement conditions (mean: $F=4.0$, $d.f.=2$, 33 , $P<0.03$). However, the mutual information was not differentially affected across reinforcement conditions for the different groups (mean: $F=0.8$, $d.f.=4$, 66 , $n.s.$). At the post hoc test, deficit patients exhibited higher mutual information than controls and nondeficit patients in condition 1 (50/50%, deficit vs. controls: $F=4.1$, $d.f.=1$, 33 , $P<0.05$; deficit vs. nondeficit: $F=4.9$, $d.f.=1$, 33 , $P<0.03$), 2 (20/80%, deficit vs. controls: $F=4.9$, $d.f.=1$, 33 , $P<0.03$; deficit vs. nondeficit: $F=8.2$, $d.f.=1$, 32 , $P<0.007$). Deficit schizophrenia showed also a statistical trend for the condition of higher mutual information compared to controls on condition 3 (80/20%, deficit vs. controls: $F=3.4$, $d.f.=1$, 33 , $P<0.07$) (Fig. 4).

3.2.6. Cross-mutual information

The degree to which the previous location of the stimulus is able to predict the current response did not differ between the groups (mean: $F=2.4$, $d.f.=2$, 33 , $n.s.$). In addition, there was no differential effect of the reinforcement condition across groups on the ability of the presentation of the previous stimulus to predict the current response (interaction: $F=0.7$, $d.f.=4$, 66 , $n.s.$).

3.2.7. Win-stay/lose-shift

Using the strategy 'win-stay/lose-shift', there was no difference (mean: $F=2.7$, $d.f.=2$, 33 , $n.s.$) between the subgroups. This behaviour for the different reinforcement conditions was not differentially affected across groups (interaction: $F=0.8$, $d.f.=4$, 66 , $n.s.$).

3.2.8. Responses bias measures

The reaction time did not differ (mean: $F=0.7$, $d.f.=2$, 33 , $n.s.$). There was no interaction between

groups and condition in reaction time ($F=1.5$, $d.f.=4$, 66, n.s.). There was no statistical significance in different latencies of decision (mean: $F=1.1$, $d.f.=2$, 33, n.s.). The latency of decision was not differentially affected across reinforcement conditions ($F=1.8$, $d.f.=4$, 66, n.s.).

3.2.9. Probability to right

In each subgroup, the patients and control subjects pressed the right and the left mouse button equally often (mean: $F=2.0$, $d.f.=2$, 33, n.s.; mean probability of 0.53 to press right and 0.47 to press left). The probability to press right for the different reinforcement conditions was not differentially influenced across groups ($F=1.3$, $d.f.=4$, 66, n.s.).

3.2.10. Switch/stay

The probability to alternate between responses on successive trials, i.e. left–right or right–left, did not differ across deficit and nondeficit schizophrenia patients or controls (mean: $F=2.0$, $d.f.=2$, 33, n.s.). Moreover, the reinforcement conditions did not differentially affect the probability of response switching across the groups (interaction: $F=0.5$, $d.f.=4$, 66, n.s.).

3.2.11. Correlations

Neither clinical symptoms nor sociodemographic information predicted performance on the two-choice task as measured by dynamical entropy, mutual information, or degree of dysregulation. Thus, there were no correlations between clinical symptoms and choice measures.

4. Discussion

In this study, we replicated the previous finding of dysregulated decision-making in a different sample of schizophrenia patients (Paulus et al., 1994, 1996). In addition, however, the current results extend previous findings in two ways: First, significant dysregulation during decision-making in the two-choice prediction task was found in deficit but not nondeficit schizophrenia patients. Second, the influence of the error rate, i.e. the reinforcement conditions, on the decision-making

behaviour of schizophrenia patients relative to that on normal comparison subjects was similar.

Decision-making is an important function of everyday life but is a complex process that involves attention, working memory, and other executive processes. Previous studies had shown that deficit-syndrome schizophrenia patients show profound deficits in cognition, e.g. attention and executive function (Buchanan et al., 1994, 1997; Bryson et al., 2001). Therefore, the dysregulation of decision-making is consistent with other cognitive dysfunctions in these patients. The response sequences generated by deficit-syndrome schizophrenia patients support this hypothesis and reveal an increased oscillation between highly predictable and highly unpredictable response sequences (dysregulation). A high degree of dysregulation of decision-making is consistent in two processes: First, subjects switch infrequently but ‘abruptly’ from one strategy to another, which leads to highly unpredictable sub-sequences. This specific behaviour in deficit patients may reflect the inability to continually update behavioural strategies. Although, the influence of the previous stimulus on the current response did not differ across patients or between patients and controls, the degree to which the previous response influenced the current response was significantly higher in schizophrenia patients relative to controls. Thus, the inability to continually update decision-making strategies may be due to the fact that the previous response exerts too much influence on the response selection process. Computationally, this dysregulation may reflect an intermittent dysfunction of the underlying neural system (Paulus et al., 1999). In addition, the response sequences of deficit-syndrome schizophrenia patients were characterized by lower metric entropy, which is consistent with a reduced utilization of possible strategies in an attempt to correctly predict the stimulus. Clinically, this behaviour in the task is comparable to repetitive acts and ideas and a loss of alternative strategies. Finally, the high mutual information among responses generated by deficit-syndrome schizophrenia patients indicates that the current response is highly dependent on the preceding response irrespective of the outcome of the previous trial. The reduced dependency of external

stimuli or outcomes in this patient group is consistent with the notion of autistic behaviour, i.e. an increased self-absorption and inability to interact socially. The combination of dysregulation, low metric entropy, and high mutual information of the dynamical process underlying decision-making in deficit-syndrome schizophrenia patients is consistent with Bleuler's original conceptualisation of autism in schizophrenia. In summary, the temporal dynamics of decision-making in deficit-syndrome schizophrenia patients is best described as an intermittent, perseverative, autistic process with infrequent bursts of unpredictable responses.

Apart from the profound dysfunctions in the sequential organization of decision-making, different levels of reinforcement had similar effects in deficit and nondeficit-syndrome schizophrenia patients compared with control subjects. The reinforcement-dependent modulation of the decision-making strategies during this task helps to separate the concept of dysregulation from lack of attention. Specifically, a switch between highly predictable and highly unpredictable response sequences could be due to the fact that the subject attends intermittently to the task. Intermittent attention to the task, however, would be inconsistent with the sensitive change of basic response biases (e.g. increased response switching during the 20% reinforcement condition). Therefore, the reinforcement-dependent response modulation supports the idea that all the subjects attend similarly to the task but the deficit-syndrome schizophrenia patients show a temporal dysregulation of strategy generation. Interestingly, during the high reinforcement condition (80%), the degree of dysregulation in deficit-syndrome schizophrenia patients did not differ significantly from that of nondeficit patients or controls. This 'normalization' of dysregulation at the higher reinforcement condition may indicate that the dynamical dysregulation shows a certain plasticity that can be used to determine which neural system underlies this dysfunction. Moreover, the plasticity of the dynamical characteristics of the behaviour with different reinforcement conditions supports the idea that the dysregulation is not related to an idiosyncratic response to reinforcement. This is consistent with the finding that the reinforcement–response relationships are relatively preserved in

schizophrenia patients (Wilder et al., 1998). There were no differences between groups in win-stay/lose-shift behaviour, switch/stay behaviour (simple perseveration) and the probability to press right or left, which supports the hypothesis that the dynamical aspects, but not the general response biases, of decision-making are dysfunctional in deficit-syndrome schizophrenia patients. These dynamical aspects of decision-making may provide a unique window into the temporal architecture of behaviour in schizophrenia patients and could be examined only with the help of a nonlinear method.

The symptom and treatment levels did not correlate significantly with decision-making characteristics in schizophrenia patients. The absence of a correlative relationship between clinical symptoms and treatment variables needs to be interpreted cautiously because these conditions were not controlled a priori. There is increasing evidence that cognitive dysfunction is a more reliable and sensitive predictor of long-term outcome than clinical symptomatology (Green, 1996). The treatment conditions reported here varied significantly; thus, a lack of correlation may be due to the limited power available with the current sample.

The major finding of this study is the establishment of a relationship between differences in decision-making and the presence of the deficit or nondeficit syndrome in schizophrenia. This finding is in agreement with a recent study in deficit and nondeficit syndrome schizophrenia, which found an impairment of executive function measured by the Wisconsin Card Sorting Test in deficit schizophrenia (Bryson et al., 2001). In contrast to a homogenous entity, it is possible to differentiate schizophrenia by syndrome levels. However, these ratings appear to be less sensitive to neurobiological correlates (Arango et al., 2000). This fine-grained behavioural analysis between deficit and schizophrenia patients may help in understanding the fundamental behavioural deficit underlying the deficit syndrome in schizophrenia.

There are several limitations in this study. First, deficit patients exhibited a higher duration of illness. Second, to get well-matched groups, we had to reduce the number of subjects; therefore, the groups are small, and null results could be due

to limited power. Third, the absence of measurement of IQ or education level is a limitation of this study. Fourth, we could not control the antipsychotic treatment; therefore, more deficit patients received typical antipsychotics ($N=7$), whereas most nondeficit schizophrenia patients received atypical antipsychotics ($N=7$). Fifth, it is unclear whether the ‘dysregulation’ of decision-making is specific to schizophrenia patients or even to deficit syndrome patients. Preliminary studies indicate that neither unipolar nor bipolar depressed patients exhibit a similar dysregulation (Paulus, 1998). However, future studies need to further explore the specificity of this finding.

In summary, an intermittent, perseverative, autistic process with infrequent bursts of unpredictable responses characterizes the decision-making in deficit schizophrenia patients. In comparison, the decision-making of nondeficit schizophrenia patients did not differ significantly from that of healthy controls. The use of a simple computerized task and the nonlinear analysis approach provide a unique window into the temporal architecture of behaviour of schizophrenia patients. The discrimination between deficit and nondeficit syndrome schizophrenia patients is the first step to determine whether decision-making dysfunctions are an intermediate phenotype in schizophrenia that can be used to better understand the heterogeneity of this disorder. Future longitudinal studies will enable us to evaluate whether dysregulation of decision-making is predictive of future deficit outcome.

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