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Journal of Affective Disorders 76 (2003) 183–189

JOURNAL OF
**AFFECTIVE
DISORDERS**

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Research report

Decision-making strategies by panic disorder subjects are more sensitive to errors

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Received 15 August 2001; received in revised form 8 March 2002; accepted 11 March 2002

Abstract

Background: Decision-making is a complex process, which can be assessed experimentally by the two-choice prediction task. Error-rate, i.e. the frequency of incorrect predictions during this task, is an important factor for the response selection during decision-making. This investigation examined whether the frequency of incorrect predictions has an augmented effect on the number of different strategies underlying decision-making in patients with panic disorder. **Methods:** Patients with a DSM-IV diagnosis of panic disorder (PD; $N = 18$), unipolar major depressive disorder (MDD; $N = 18$) and normal comparison subjects (C; $N = 35$) were tested with the two-choice prediction task using three error-rate conditions (20, 50, or 80%). The dynamical entropy of the response sequences was used to quantify the number of different strategies generated during the different error-rates. **Results:** At 20% error-rates, panic disorder subjects when compared to MDD and C subjects generated more strategies and switched more frequently between strategies as measured by the dynamical entropy and the range of local dynamical entropies. Response bias measures during the two-choice prediction task and post-test self-assessment did not differ between panic disorder subjects and MDD or C subjects. **Limitations:** First, panic disorder subjects were medicated. Second, the frequency and intensity of panic attacks and the degree of avoidance behaviors, was not assessed. Third, subjects were tested once only. **Conclusions:** Panic disorder subjects show uniformly high response sequence unpredictability in the presence of low error-rates, which is consistent with continued search for an optimal response strategy even when the error-rate is low.

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Keywords: Panic disorder; Decision-making; Reinforcement; Cognitive dysfunction

1. Introduction

The evaluation and amplification of low-level somatic sensations in the cognitive and affective

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context of high anxious apprehension via a disinhibited feedback of threat-associated perceptual cues, has been proposed as a key process in the development of panic disorder (Barlow, 1988; Chambless et al., 2000; Gorman et al., 2000). An increased sensitivity of the amygdala (LeDoux, 2000) and temporo-hippocampal structures (Reiman et al., 1984; Nordahl et al., 1990) in response to these cues has been hypothesized to contribute to this disinhibition. Psychological and cognitive theories of panic disorder relate the escalation of anxiety (Clark, 1986; Ehlers et al., 1988; Beck and Clark, 1997; Windmann, 1998) to the misinterpretation of perceptual cues based on an attentional bias towards threat (Reiss and McNally, 1985; McNally et al., 1994). These approaches, however, have focused primarily on perceptual cues or attentional biases in patients with panic disorder. The consequences of these processes for the selection of action (i.e. choosing between different possible responses) and decision-making cognition have been less well studied.

Decision-making is a complex process that occurs whenever a person selects an action in the presence of an uncertain outcome (Tversky and Kahneman, 1981). In a simple decision-making paradigm, the two-choice prediction task, subjects are asked to repeatedly predict the location of a stimulus on a computer screen. When asked to select between response alternatives subjects will generally select the action which is most likely associated with the 'correct' outcome (Calfee and Atkinson, 1966; Ludvigson, 1966; Goulet and Barclay, 1967). This behavior corresponds to the well-known matching law that has been observed in a large number of animal studies (Herrnstein, 1997). Several psychological models have been proposed to explain how response selection depends on reinforcement history, even in the presence of random reinforcement (Resstle, 1966; Rose and Vitz, 1966). Central to these models is the notion that the subject maintains a representation of the history of 'correct' vs. 'incorrect' decisions and adjusts his/her strategies accordingly. Therefore, the decision-making process is influenced in a complex manner by the history of success or failure previous actions.

This investigation examined whether the frequency of incorrect predictions, i.e. the error-rate, has an augmented effect on the number of different strategies underlying decision-making in patients

with panic disorder. Using the two-choice prediction task, the frequency of correct or incorrect predictions can be determined a-priori, which allows one to examine how decision-making changes as a function of error-rate. The number of different strategies underlying response selection during decision-making can be quantified comprehensively using non-linear techniques (Paulus et al., 1997). Specifically, the dynamical entropy (Eckmann and Ruelle, 1985) quantifies the degree to which sequences of actions can be predicted. For example, an increased number of strategies decreases the predictability of actions sequences during decision-making and, therefore, increases the dynamical entropy. The dynamical entropy reveals a high degree of unpredictability when subjects correctly predict 50% of the stimuli during the two-choice prediction task. In comparison, the number of different strategies as measured by the dynamical entropy decreases significantly when subjects correctly predict 80% of the stimuli, i.e. the number of different strategies decreases as the number of correct prediction increases. Thus, an increased sensitivity to errors in panic disorder patients relative to normal comparison subjects should result in an increased number of strategies underlying the response sequences during the two-choice prediction task particularly at low error-rates.

2. Method

The experiment was approved by the Psychiatric Services of Aargau Canton Human Subject Committee. Eighteen subjects with panic disorders (PD: 36 ± 11.5 years, range: 22–61 years; eight men, 10 women) were compared with 18 age-matched unipolar major depressive disorder subjects (MDD: 42 ± 12.5 years, range: 17–58 years; 10 men, eight women) and 35 age-matched normal comparison subjects (C: 39 ± 14.1 years, range: 21–68 years; 20 men, 15 women). Patients were recruited via the Inpatient Psychiatric Services of Aargau Canton (Switzerland). Comparison subjects were recruited from hospital employees or via local advertisements. A semi-structured interview was conducted with the patient groups and the comparison group. PD and MDD subjects were diagnosed according to DSM-IV diagnostic criteria. Normal comparison subjects did

not have a history of psychiatric disorder, substance abuse, or major medical disorder.

Symptom ratings included the symptom checklists (SCL-90; Derogatis et al., 1976; Global Severity Index: PD: mean 1.6 ± 0.8 ; MDD: mean 1.4 ± 0.6 ; C: mean 0.3 ± 0.3). Anxiety symptoms were rated in panic patients with the Hamilton Anxiety Scale (HAMA; Hamilton, 1969; TOTAL: mean 30 ± 7.7), the State Trait Anxiety Inventory (STAI; Spielberger et al., 1970; STATE: mean 49.4 ± 10.2 ; TRAIT: mean 53.3 ± 10.3).

The two-choice prediction task has been described in detail elsewhere (Paulus et al., 1997). Briefly, a house flanked by a person to the left and right is shown on a computer screen. The subject is instructed to 'predict' whether a car will be shown on the left or right side of the computer screen and to press a left or right button so that the person on the screen can meet up with a car. AFTER the subject has made a response, the car is presented for 300 ms on the far left or right side. Unbeknownst to the subject, a computer program, which takes the response of the subject into account, determines a priori whether a response will be 'correct' or 'incorrect'. The two-choice prediction task was divided into three trial-blocks. During the first trial-block, which consisted of 128 trials, the computer program assured that 50% of all responses were 'correct' (50% error-rate), during the second trial-block corresponding to the next 64 trials 20% of all responses 'correctly predicted' the location of the car (80% error-rate), and during the third trial-block, which comprised the next 64 trials, 80% of all responses were 'correct' predictions (20% error-rate). The basic variables are the subject's response, the location of the car, and the latency to select a response, i.e. the time from the beginning of the trial to the button press.

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; and (3) the current response was part of a highly predictable or highly unpredictable response sequence. First, response bias measures quantified 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 (Herzel and Grosse, 1995) quantifies the predictability of the current response by the previous response. In addition, the cross-mutual information (CMI) quantifies the predictability of the current response by the previous stimulus, i.e. whether the car was presented on the LEFT or RIGHT side on the previous trial. Third, the dynamical entropy was computed from the sequences of responses to quantify the degree of response sequence predictability. This measure quantifies the rate of the number of different response sequences as a function of sequence length. Specifically, a highly unpredictable response sequence is characterized by the fact that similar response sequences cannot be used to successfully predict the next response. The range of response sequence predictability (difference between the most unpredictable and most predictable response sequence) quantifies how frequently the subjects switch between different strategies. These behavioral 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).

2.1. Statistics

All statistical analyses were performed using STATISTICA/w™ (StatSoft™). For the statistical analyses a mixed ANOVA with subject group as a between- and reinforcement-condition as a within-factor was used.

3. Results

The first set of analyses examined whether basic response characteristics during the two-choice prediction task differed across panic disorder, major depressive disorder, or normal comparison subjects. All subjects selected approximately equally likely the LEFT or RIGHT response (probability of selecting the RIGHT response: PD = 0.52, MDD = 0.51, C = 0.51). As expected, the higher the error-rate the greater the switching rate from the current response

to the alternative response ($F = 20.0$, $df = 2,134$, $P < 0.01$). The switching rate was not differentially affected as a function of error-rate across groups, i.e. both panic disorder and normal comparison subjects increased switching similarly with increased error-rates ($F = 0.4$, $df = 2,67$, n.s.)

The second set of analysis examined whether the response selection by panic disorder subjects was significantly more affected by the previous response or the previous stimulus. The degree to which the previous response or the previous stimulus predicted the current response differed significantly across error-rate conditions (MI: $F = 9.3$, $df = 2,136$, $P < 0.01$, CMI: $F = 4.2$, $df = 2,136$, $P < 0.05$) but not across groups (MI: $F = 0.7$, $df = 2,68$, n.s., CMI: $F = 0.3$, $df = 2,68$, n.s.) or differentially across groups in different error-rate conditions (MI: $F = 1.8$, $df = 4,136$, n.s., CMI: $F = 1.5$, $df = 4,136$, n.s.). Specifically, both the previous response and the previous stimulus were more predictive of the current response during 20% error-rate relative to the 50% error-rate condition. Thus, PD subjects did not differ from MDD or normal comparison subjects when selecting the current response in relation to the previous stimulus or response.

The third set of analyses examined whether the number of different strategies and the degree with which subjects switched between different strategies differed across PD, MDD, or C subjects. Overall, the average dynamical entropy of the response sequences did not differ significantly across groups ($F = 2.5$, $df = 2,67$, n.s.). Different error-rate conditions, however, significantly affected the average response sequence predictability ($F = 21$, $df = 2,134$, $P < 0.01$). Moreover, PD, MDD, and C subjects differed significantly across different error-rate conditions ($F = 3.2$, $df = 4,134$, $P < 0.01$; Fig. 1). Specifically, the sequences of both normal comparison and MDD subjects were more predictable at low error-rates (20% error-rate: PD-C: $F = 11.7$, $df = 1,67$, $P < 0.001$; PD-MDD: $F = 5.3$, $df = 1,67$, $P < 0.02$). In contrast, panic disorder patients showed a similar level of predictability across all error-rates.

Overall, the degree to which subjects switched between different strategies did not differ across groups ($F = 0.9$, $df = 2,67$, n.s.). Error-rates significantly affected the range of response sequence predictabilities ($F = 7.2$, $df = 2,134$, $P < 0.01$).

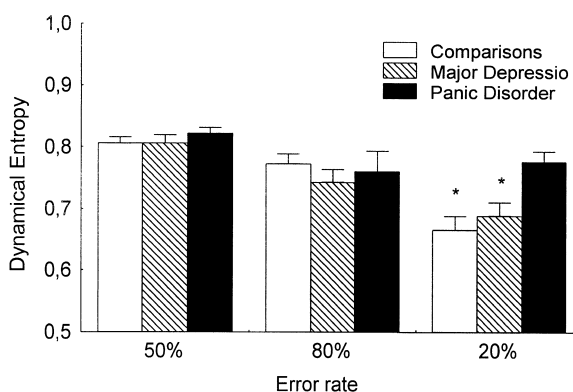


Fig. 1. Panic disorder patients exhibit significant higher dynamical entropy during the 20% error-rate condition compared to patients with major depression and comparison subjects.

Moreover, the degree with which subjects switched between strategies in different error-rate conditions differed across PD, MDD and C subjects ($F = 3.4$, $df = 4,134$, $P < 0.05$). Whereas both normal comparison and MDD subjects showed an increase in non-uniformity (or increased dysregulation, Paulus et al., 1997) at low error-rates, panic disorder subjects showed a similar range of response sequence predictability across error-rates (PD-C: $F = 8.6$, $df = 1,67$, $P < 0.005$; PD-MDD: $F = 4.6$, $df = 1,67$, $P < 0.04$; Fig. 2).

Performance during the two-choice prediction task quantified by response bias measures, mutual in-

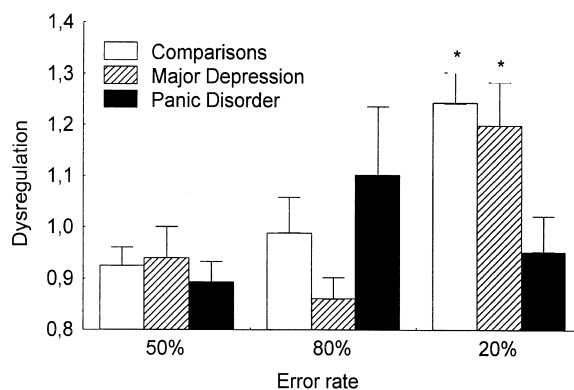


Fig. 2. Dysregulation (max.-min. entropy) for comparison subjects, patients with major depression and panic disorder; panic patients show decreased dysregulation during the 20% error-rate condition.

formation functions, and the dynamical entropy analysis were not correlated with measures of state or trait anxiety, symptoms of depression or SCL-90 factors (data not shown). A self-report post-task questionnaire indicated that it was important for all subjects to correctly predict the location of the stimulus (PD-C: $\chi^2 = 2.9$, $df = 2$, n.s.). Moreover, all groups similarly perceived their performance on this task (PD-C: $\chi^2 = 1.0$, $df = 2$, n.s.). Relative to normal comparison subjects, depressive (MDD-C: $\chi^2 = 6.3$, $df = 2$, $P < 0.05$) and panic (PD-C: $\chi^2 = 8.2$, $df = 2$, $P < 0.02$) disorder subjects, however, reported more tension during the task.

4. Discussion

This study yielded two main results. First, panic disorder subjects but not MDD or normal comparison subjects showed a similar level of response sequence unpredictability and range of response sequence predictabilities across the different error-rates. Specifically, at low error-rates panic disorder subjects relative to both MDD and C subjects generated less predictable response sequences and switched more frequently between underlying strategies. Second, panic disorder subjects did not differ from MDD or C subjects on measures of simple response bias and response or stimulus related response selection across error-rates. These results are consistent with the hypothesis that the frequency of incorrect predictions, i.e. the error-rate, has an augmented effect on the number of different strategies underlying decision-making in patients with panic disorder.

The controlled manipulation of the error-rate in the two-choice prediction task enables one to determine how success or failure influences response bias, stimulus-response and response rigidity, and strategy selection during decision-making. The lack of error-rate related differences in response biases between panic disorder subjects and MDD or normal comparison subjects supports the hypothesis that error-rates do not differentially bias these subjects. In comparison, the error-rate related differences between panic disorder subjects and MDD or normal comparison subjects for the dynamical entropy and the range of response sequence predictability is

consistent with a disruption of a dynamical process that relates success to strategy selection during decision-making. Thus, an increased sensitivity to errors in panic disorder patients relative to normal comparison subjects may prompt these subjects to continue to ‘search’ for different response sequences even when the selected response is ‘correct’ in approximately 80% of the trials.

Previous neuroimaging studies using various forms of a two-choice task have shown that a system of fronto-parietal and cingulate cortex is critically involved in the decision-making process (Elliot and Dolan, 1998; Paulus et al., 2001). This system receives modulating input from the limbic and paralimbic system (Mesulam, 1998) including the amygdala. Moreover, the amygdala and prefrontal cortex are interconnected, and activity in one region may influence the other during cognition, as illustrated by amygdala modulation of prefrontal cortex activity during fear conditioning (Garcia et al., 1999). Thus, it is conceivable that an error-dependent activation of the amygdala affects the ongoing processing of alternative strategies during the two-choice prediction task such that panic disorder subjects switch more frequently among competing strategies. Thus, future studies will examine the relationship between activation of the amygdala and reinforcement conditions during the two-choice prediction task in subjects with panic disorder to examine the hypotheses of differentially increased amygdala activation during the low error-rate condition.

This study has several limitations. First, 14 of 18 subjects with panic disorder were medicated with a number of different substances including SSRIs and TCAs. Although subjects with MDD treated with similar medications did not show the low error-rate decision-making dysfunctions, one cannot rule out that disorder-specific medication effects contributed to the current pattern of results. Second, the severity of panic disorder, e.g. as measured by the frequency and intensity of panic attacks or the degree of avoidance behaviors, was not assessed in this study. Therefore, we cannot conclude that the decision-making dysfunctions are related to the severity of the clinical syndrome of panic disorder. Third, subjects in this study were tested once only. Therefore, it is unclear whether this deficit is a trait or state-like

characteristic. Fourth, the sequence of error-rate conditions was not randomised across subjects. Future studies will need to examine the stability of the decision-making dysfunctions across time and across different illness stages.

In conclusion, panic disorder subjects show high response sequence unpredictability at low error-rates, which is consistent with continued search for an optimal response strategy even when subject's predictions are frequently correct. This finding is consistent with a dysfunction of decision-making cognition in panic disorder subjects that differs from that previously seen in schizophrenia patients (Paulus et al., 1999). One possible clinical implication is that the increased error sensitivity lead to anxious hyperarousal when panic disorder patients select an action with an adverse outcome, which could promote the development of panic symptoms and associated avoidance behaviors. If this hypothesis is correct, one would predict that panic disorder subjects with a high degree of error sensitivity as measured by the difference in dynamical entropy at low and high error-rates show more severe panic symptoms or more extensive avoidance behaviors. Future investigation will need to be conducted to examine this question.

Acknowledgements

Supported in part by Organon, Switzerland.

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