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## General functioning predicts reward and punishment learning in schizophrenia

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### ABSTRACT

Previous studies investigating feedback-driven reinforcement learning in patients with schizophrenia have provided mixed results. In this study, we explored the clinical predictors of reward and punishment learning using a probabilistic classification learning task. Patients with schizophrenia ( $n=40$ ) performed similarly to healthy controls ( $n=30$ ) on the classification learning task. However, more severe negative and general symptoms were associated with lower reward-learning performance, whereas poorer general psychosocial functioning was correlated with both lower reward- and punishment-learning performances. Multiple linear regression analyses indicated that general psychosocial functioning was the only significant predictor of reinforcement learning performance when education, antipsychotic dose, and positive, negative and general symptoms were included in the analysis. These results suggest a close relationship between reinforcement learning and general psychosocial functioning in schizophrenia.

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### 1. Introduction

In one of the most fundamental forms of learning, humans acquire stimulus–response associations based on trial-to-trial feedback (reward or punishment) after each response. Several previous studies have attempted to investigate this type of feedback-driven reinforcement learning in schizophrenia, but the results are heterogeneous and non-conclusive, with some studies showing an impairment and others showing no impairment (for a comprehensive review and synthesis, see Gold et al., 2008, 2009). Several variables may contribute to the diversity of results, including differences in symptom severity and type of symptom-dimensions across the patients

being studied. For example, in a group of highly-functioning outpatients with schizophrenia, we found intact feedback-driven learning (Kéri et al., 2000), whereas in more severely affected patients with prominent primary negative symptoms, we observed significant impairments (Farkas et al., 2008; Polgár et al., 2008). Waltz et al. (2007) found that patients with schizophrenia are able to use negative feedback during procedural learning, but their ability to use positive feedback is disrupted, which is associated with negative symptoms. Weiler et al. (2009) demonstrated a similar reward-based learning deficit in patients with schizophrenia who exhibited a comparable level of negative symptoms to those included in our studies (Farkas et al., 2008; Polgár et al., 2008). Weiler et al. (2009) also showed that reward-learning impairment cannot be explained by lower levels of IQ and working memory, which are only weakly related to reinforcement learning.

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Another potential confounding variable is the presence, degree, and type of antipsychotic medication. Beninger et al. (2003) reported that patients receiving first-generation antipsychotics show disrupted feedback-driven learning, which was replicated by Kéri et al. (2005) using another feedback-based learning task. Harris et al. (2009) found spared procedural learning in drug-naïve patients with schizophrenia, which was disrupted by antipsychotic medications. A plausible explanation may be that strong dopamine receptor antagonists interfere with reward-processing (Pessiglione et al., 2006), which may contribute to deficient feedback processing and procedural learning. Most antipsychotic medications target dopamine D2 receptors, which were found to be key for reward processes (Drew et al., 2007; Laviolette et al., 2008).

Although it has been emphasized that general functioning of patients with schizophrenia is strongly influenced by cognitive deficits representing a key target for future treatment (Green et al., 2004; Keefe, 2007), the role of feedback-driven reinforcement learning is unknown, especially in relation to clinical symptoms and antipsychotic medications. The most widespread tool to assess general psychosocial functioning, in addition to the overall severity of symptoms, is the Global Assessment of Functioning (GAF) scale, which is coded on the Axis V of the DSM-IV (American Psychiatric Association, 1994). In contrast to the multidimensional clinical evaluation of symptoms, such as the Positive and Negative Syndrome Scale (PANSS), the GAF characterizes how illness influences community, family, and occupational functioning in the everyday life of the patients.

In this study, we tested the hypothesis that GAF is a significant predictor of feedback-driven reinforcement learning in schizophrenia when education, symptoms, and antipsychotic medications are taken into consideration. In addition, based on our previous findings of impaired associative learning in deficit but not in non-deficit patients (Farkas et al., 2008; Polgár et al., 2008), we hypothesized that patients with severe negative symptoms will show impairment at basal ganglia-based behavioral tasks, such as learning from reward, but not from punishment (Waltz et al., 2007, 2009).

## 2. Methods

### 2.1. Participants

Participants were 40 patients with schizophrenia (22 outpatients) and 30 healthy control volunteers with negative psychiatric history. The patients were recruited at the Semmelweis University, Department of Psychiatry and Psychotherapy. The inpatients participated in a psychosocial rehabilitation program and were not in an acute psychotic state at the time of testing. The control volunteers were employees and their acquaintances who were matched with the patients for age, gender, and education (Table 1). The diagnosis was based on the DSM-IV criteria (American Psychiatric Association, 1994). All participants received the International Neuropsychiatric Interview Plus (Sheehan et al., 1998). Detailed medical records were available from all patients. Persons with alcohol and drug abuse were excluded from the study. General functioning was assessed with the GAF scale (American Psychiatric Association, 1994). Clinical

**Table 1**

Demographic and clinical characteristics of the participants.

	Schizophrenia (n = 40)	Controls (n = 30)
Male/female	17/23	10/20
Age (years)	36.6 (10.0; 22–59)	37.0 (9.6)
Education (years)	12.4 (2.4; 8–18)	12.6 (2.7)
Duration of illness (years)	8.0 (6.6; 1–25)	–
Number of episodes	5.6 (4.3; 1–14)	–
GAF	54.7 (17.1; 25–90)	–
PANSS positive	12.0 (4.6; 7–23)	–
PANSS negative	15.6 (6.8; 7–32)	–
PANSS general	27.3 (8.2; 18–45)	–

Data are mean (standard deviation; range). GAF – Global Assessment of Functioning, PANSS – Positive and Negative Syndrome Scale.

symptoms were evaluated with the PANSS (Kay et al., 1987) (Table 1). These scales were administered by trained clinicians (Z.S. and S.K.) who were blind to reward- and punishment-learning data at the time of clinical assessment (inter-rater reliability: Cohen's kappa and  $r \geq 0.7$ ). The assessment of the patients was based on individual interviews with the patients and with one of their family members. The full medical records of the patients were available. Patients and controls were matched for tobacco smoking (30% of participants were heavy smokers in both groups) because smoking may have an influence on reward learning (Yip et al., 2009).

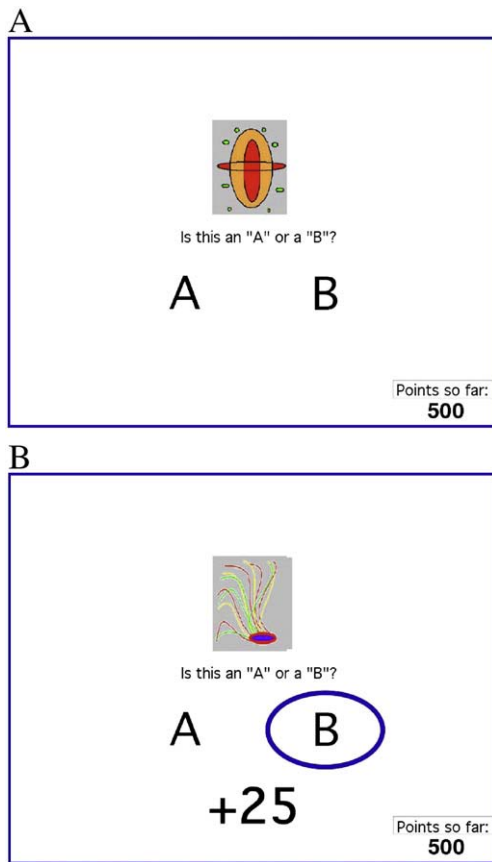
Antipsychotic medications included clozapine (n = 7), olanzapine (n = 11), risperidone (n = 8), quetiapine (n = 3), aripiprazole (n = 5), sertindole (n = 3), amisulpride (n = 2), haloperidol (n = 2), flupenthixol (n = 4). Six patients received combinations of two antipsychotics, and one patient did not receive medications at the time of testing. The average daily value of chlorpromazine-equivalent antipsychotic dose was 363.4 mg (SD = 232.4) (Woods, 2003).

The study was approved by the local ethics board. After complete description of the study, written informed consent was obtained.

### 2.2. Feedback-guided reinforcement learning

We used the same procedure that was introduced by Bódi et al. (2009) in the assessment of patients with Parkinson's disease. On each trial, participants viewed one of four images (S1–S4) (Fig. 1), and were asked to guess whether it belonged to category A or category B. Stimuli S1 and S3 belonged to category A with 80% probability and to category B with 20% probability, while stimuli S2 and S4 belonged to category B with 80% probability and to category A with 20% probability (Table 2). Stimuli S1 and S2 were used in the reward-learning task. In this task if the participant correctly guessed the category membership on a trial with either of these stimuli, a reward of +25 points was received; if the participant guessed incorrectly, no feedback appeared. Stimuli S3 and S4 were used in the punishment-learning task. In this task if the participant guessed incorrectly on a trial with either of these stimuli, a punishment of –25 was received; correct guesses received no feedback.

The experiment was conducted on a Macintosh i-book, programmed in the SuperCard language (Allegiant Technologies, San Diego, CA). The participant was seated in a quiet



**Fig. 1.** A screen shot of the reward-punishment task used in the present study. (A) On each trial, the participant saw one of four abstract shapes and was asked whether this shape belonged to category A or B. (B) For some stimuli, correct responses were rewarded with visual feedback and 25 points winnings, whereas for others, incorrect responses were punished with a loss of 25 points.

testing room at a comfortable viewing distance from the screen. The keyboard was masked except for two keys, labelled “A” and “B” which the participant could use to enter responses. Before the experiment, the participant received the following instructions: “In this experiment, you will be shown pictures, and you will guess whether those pictures belong to category “A” or category “B”. A picture does not always belong to the same category each time you see it. If you guess correctly, you may win points. If you guess wrong, you may lose points. You will see a running total of your points as you play. We will start you off with a few points now. Press the mouse button to begin practice.”

In the practice phase, the participant received sample trials from the punishment- and reward-learning tasks. The

practice stimuli were not included in the experiment. The participant saw a practice image, with a prompt to choose category A or B, and a running tally of points at the lower right corner of the screen. The tally was initialized to 500 points at the start of practice. The participant was first instructed to press the “A” key, which resulted in a punishment of  $-25$  and updated point tally and then the “B” key, which resulted in no feedback. The participant then saw a second practice figure and was instructed first to press the “B” key which resulted in a reward of  $+25$  and updated point tally and then the “A” key, which resulted in no feedback.

After these two practice trials, a summary of instructions appeared: “So... For some pictures, if you guess CORRECTLY, you WIN points (but, if you guess incorrectly, you win nothing). For other pictures, if you guess INCORRECTLY, you LOSE points (but, if you guess correctly, you lose nothing). Your job is to win all the points you can – and lose as few as you can. Remember that the same picture does not always belong to the same category. Press the mouse button to begin the experiment.” From here, the experiment began. On each trial, the participant saw one of the four stimuli (S1, S2, S3, or S4) and was prompted to guess whether it was an “A” or a “B”. On trials in the reward-learning task (with stimuli S1 or S2), correct answers were rewarded with positive feedback and gain of 25 points; incorrect answers received no feedback. On trials in the punishment-learning task (with stimuli S3 or S4), incorrect answers were punished with negative feedback and loss of 25 points; correct answers received no feedback. The no-feedback outcome was thus ambiguous, as it could signal lack of reward (if received during a trial with S1 or S2) or lack of punishment (if received during a trial with S3 or S4).

The task contained 160 trials, divided into 4 blocks of 40 trials each. Within a block, trial order was randomized. Training on the reward-learning task (S1 and S2) and punishment-learning task (S3 and S4) were intermixed. Within each block, each stimulus appeared 10 times, 8 times with the more common outcome (e.g. category “A” for S1 and S3 and “B” for S2 and S4) and 2 times with the less common outcome. Trials were separated by an interval of 2 seconds, during which time the screen was blank.

At the end of the 160 trials, if the participant’s running tally of points was less than 525 (i.e. no more than the 500 points awarded at the start of the experiment), additional trials were added on which the participant’s response was always taken as correct, until the tally was at least 525. This was added in order to minimize frustration in participants by ensuring that all participants terminated the experiment with more points than they had started with. Data from any such additional trials were not analyzed. On each trial, the computer recorded whether the participant made the optimal response (i.e. category A for S1 and S3, and category B for S2 and S4), regardless of actual outcome.

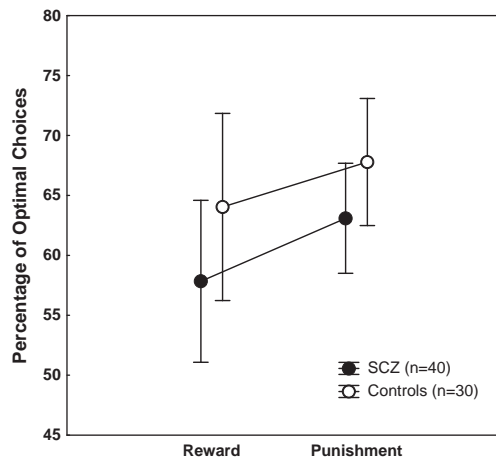
### 2.3. Data analysis

The STATISTICA 8.0 package was used for data analysis (StatSoft, Inc., Tulsa). The data were entered into Kolmogorov–Smirnov tests in order to check the normality of distribution. The main dependent measure was the percentage of optimal choices from the reward- and punishment-learning tasks. First, an analysis of variance (ANOVA) was

**Table 2**

Category and feedback structure of the probabilistic classification task.

Stimulus	Probability class A	Probability class B	Feedback
S1	80%	20%	If correct: $+25$
S2	20%	80%	If incorrect: $\emptyset$
S3	80%	20%	If correct: $\emptyset$
S4	20%	80%	If incorrect: $-25$



**Fig. 2.** Experimental results on reward and punishment trials in healthy controls and patients with schizophrenia (SCZ). Error bars indicate 95% confidence intervals.

used to compare patients with schizophrenia and healthy controls. In this ANOVA, group (patients vs. controls) was the between-subject factor and feedback-type (reward vs. punishment) was the within-subject factor. Pearson's correlation coefficients (*r*) were calculated among the variables. Multiple linear regression analyses were used to determine the predictors of reward- and punishment-learning performances. In the model, we included four potential predictors: education, chlorpromazine-equivalent daily dose of antipsychotics, GAF, and PANSS scores (positive, negative and general symptoms). The level of significance was set at  $\alpha < 0.05$ .

**3. Results**

Results from the reinforcement learning task are depicted in Fig. 2. Although patients with schizophrenia made numerically fewer optimal decisions than controls, the ANOVA demonstrated no statistically significant main effect of group ( $F(1,68) = 2.38, p = 0.13$ ). Similarly, although participants made numerically more optimal responses on punishment-learning than reward-learning trials, the effect of feedback-type was not significant ( $F(1,68) = 2.83, p = 0.10$ ). Finally, there was no interaction between group and feedback-type ( $F(1,68) = 0.08, p = 0.78$ ), suggesting no

differential impairment in schizophrenia for reward or punishment learning.

Table 3 shows the correlations among reinforcement learning, years of education, chlorpromazine-equivalent daily antipsychotic dose, GAF scores, and PANSS positive, negative and general symptoms. Among the significant correlations were a negative relationship between PANSS negative and general (but not positive) symptoms and performance on the reward-learning task: lower severity of PANSS negative/general symptoms was associated with a higher percentage of optimal decisions on the learning task. Neither negative nor general symptoms were significantly correlated with performance on the punishment-learning task.

When the percentage of optimal decisions from the reward-learning task was included in a linear regression analysis as a dependent variable, and years of education, chlorpromazine-equivalent daily antipsychotic dose, GAF scores, and PANSS positive, negative and general symptoms were included as independent variables, only the GAF scores emerged as a significant predictor of task performance ( $F(1,38) = 7.8, p = 0.008, R^2 = 0.17$ ). The other predictors were not significant (education:  $R^2 = 0.01, p = 0.5$ ; antipsychotic dose:  $R^2 = 0.02, p = 0.3$ ; PANSS positive:  $R^2 = 0.00, p = 0.8$ ; PANSS negative:  $R^2 = 0.03, p = 0.2$ ; PANSS general:  $R^2 = 0.02, p = 0.3$ ).

When the dependent variable was the percentage of optimal decision from the punishment-learning task, the significant predictive effect of the GAF scores was again observed ( $F(1,38) = 6.21, p = 0.02, R^2 = 0.14$ ). The other predictors were not significant (education:  $R^2 = 0.03, p = 0.2$ ; antipsychotic dose:  $R^2 = 0.01, p = 0.5$ ; PANSS positive:  $R^2 = 0.01, p = 0.6$ ; PANSS negative:  $R^2 = 0.03, p = 0.2$ ; PANSS general:  $R^2 = 0.03, p = 0.2$ ).

**4. Discussion**

The most important finding of this study is that feedback-driven reinforcement learning is predicted by general psychosocial functioning in patients with schizophrenia, but not by education, PANSS scores, and chlorpromazine-equivalent doses of antipsychotics. The GAF score accounted for 14–17% of variance on reinforcement learning performance (Fig. 3). This suggests the primacy of general functioning in relation to feedback-driven reinforcement learning. Although negative and general symptoms correlated only with reward learning, the GAF scores predicted both reward and

**Table 3**  
Pearson's correlation coefficients in patients with schizophrenia (n = 40).

	Reward	Punishment	Education	CPZ	GAF	Pos	Neg	Gen
Reward	–	0.12	0.19	–0.29	0.41*	–0.28	–0.38*	–0.37*
Punishment	0.12	–	0.25	–0.10	0.37*	–0.13	–0.14	–0.24
Education	0.19	0.25	–	–0.14	0.42*	–0.15	–0.49*	–0.17
CPZ	–0.29	–0.10	–0.14	–	–0.40*	0.23	0.27	0.29
GAF	0.41*	0.37*	0.42*	–0.40*	–	–0.64*	–0.76*	–0.71*
Pos	–0.28	–0.13	–0.15	0.23	–0.64*	–	0.44*	0.73*
Neg	–0.38*	–0.14	–0.49*	0.27	–0.76*	0.44*	–	0.61*
Gen	–0.37*	–0.24	–0.17	0.29	–0.71*	0.73*	0.61*	–

Reward and punishment – percentage of optimal decisions in the reinforcement learning task; CPZ – chlorpromazine-equivalent daily dose; GAF – Global Assessment of Functioning; Pos – positive symptoms on the Positive and Negative Syndrome Scale; Neg – negative symptoms, Gen – general symptoms. \* = statistically significant correlations ( $p < .05$ ).



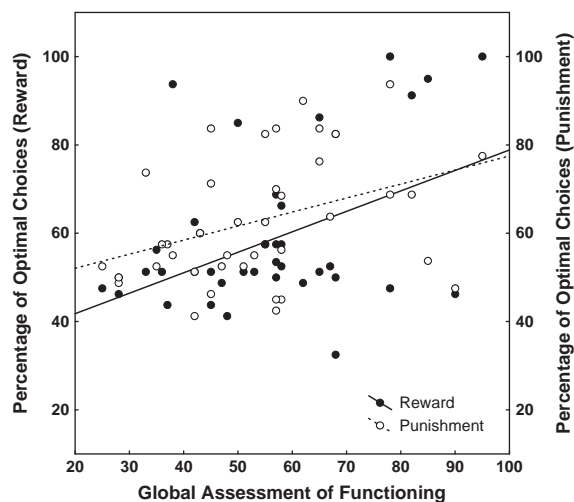


Fig. 3. Relationship between Global Assessment of Functioning scores and reinforcement learning.

punishment learning. This is particularly striking since patients with schizophrenia displayed no significant reward- or punishment-learning deficits relative to healthy controls, ruling out the possibility of non-specific factors such as fatigue or lack of motivation.

The correlation between antipsychotic dose and reward learning was in the expected negative direction (Kéri et al., 2005), but it did not reach the level of statistical significance ( $r = -0.29$ ). One possible explanation is that the majority of the patients in the current study were being treated with second-generation antipsychotics with fairly low affinity to dopamine receptors; this is in contrast to the patients included in the Kéri et al. (2005) study who dominantly received antipsychotics with higher dopamine receptor affinity. This interpretation would be consistent with the earlier finding of Bódi et al. (2009) that patients with reduced brain dopamine, due to unmedicated Parkinson's disease, show selective impairments in reward learning, which is remediated after 12 weeks of treatment with dopaminergic agonists. However, dopamine antagonist antipsychotics may improve the generalization of associations learned via feedback signals in schizophrenia (Shohamy et al., 2010).

The way patients with schizophrenia use feedback during the acquisition of stimulus–response associations is controversial: while some prior studies have indicated normal learning (Kéri et al., 2000; Weickert et al., 2002; Waltz and Gold, 2007; Murray et al., 2008a), others have found significant impairments (Foerde et al., 2008; Horan et al., 2008; Murray et al., 2008b; Weiler et al., 2009; Koch et al., 2010). Differences in patient samples discussed earlier may account for these mixed results. It is of particular importance that normal behavioral performance does not guarantee unaltered brain activation. During a probabilistic feedback-guided task on which psychotic patients showed no impairment, Murray et al. (2008a) demonstrated abnormal activation in a mesocorticolimbic network that drive reinforcement learning; it seems that patients fail to distinguish between relevant and irrelevant feedback signals. Schlagenhau

et al. (2009) found a relationship between reward-related brain activation and delusions in unmedicated patients with schizophrenia. Given the role of dopamine in reward prediction, novelty and salience, Kapur et al. (2005) postulated that psychotic symptoms arise from an aberrant assignment of salience to mental representations. Antipsychotic drugs block dopamine receptors and therefore decrease aberrant salience.

On the other hand, however, dampened response in the ventral striatum may be associated with negative symptoms (Juckel et al., 2006a; Simon et al., 2010). Weickert et al. (2009) described abnormal fronto-striatal activation in good learners of probabilistic feedback-driven associations, and Koch et al. (2010) showed that reward expectancy-related processing was associated with a hypoactivation in putamen, dorsal cingulate and superior frontal cortex in patients with schizophrenia compared to healthy controls. Antipsychotics with distinct affinities to dopamine receptors seem to differentially modulate the ventral striatal reward system, with higher affinity drugs leading to dampened response and more severe negative symptoms (Juckel et al., 2006b). It is logical to assume that the dampened activation of reward-driven brain regions is associated with less effective feedback-guided learning (Aron et al., 2004).

Although there is extensive evidence revealing that higher-level cognitive functions are related to functional outcome in schizophrenia (Green et al., 2004; Keefe, 2007), the role of more simple feedback-driven reinforcement learning is less clear. However, the above described complex mesocorticolimbic dysfunctions during reinforcement learning suggest that these may lead to anomalies in emotion, motivation and reward regulation that may result in problems in real-life general functioning (Gold et al., 2008). Kawakubo et al. (2006) demonstrated that performance on a sensory-motor task guided by feedback (Mirror Reading Test) is related to nonverbal social skills in schizophrenia. Despite the paucity of experimental evidence, reward feedback following adequate social performance is traditionally used in the psychotherapy of severe mental disorders, including schizophrenia (Dickerson et al., 2005). Silverstein et al. (2009) developed a new attention shaping method, which is based on reward learning and can successfully be used to treat highly distractible patients. Our results suggesting a prominent relationship between general functioning and feedback-driven reinforcement learning provides a theoretical background for these intervention studies implementing reinforcement learning principles in clinical practice.

The current study has two main limitations. First, psychosocial functions were evaluated only with the GAF scale, which is a rather non-specific measure. Second, there was no comprehensive neuropsychological assessment in patients with schizophrenia. However, there is evidence that higher-level cognitive functions, which are impaired in schizophrenia, are only weakly associated with simple feedback-driven reinforcement learning (Weickert et al., 2002; Kéri et al., 2005; Waltz et al., 2007; Weiler et al., 2009). Overall, further studies are warranted to explore more dimensions of psychosocial functioning (e.g. quality of life, objective functioning, and subjective well-being) and cognition and to investigate their relationship with reinforcement learning.

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**Contributors**

S.K., C.E.M., A.A.M and M.A.G. participated in study design. Z.S. conducted the experiments, performed the literature search, and analyzed the data together with A.A.M. Z.S. and S.K. wrote the first draft of the paper, and all authors contributed to the final version of the manuscript.

**Conflict of interest**

The authors declare no conflict of interest.

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None.

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