



## 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

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