Supplementary Data

Detailed Results from Experiment 1. In our first experiment, in which used Japanese Hiragana characters, SZ patients demonstrated marked impairment in the acquisition of probabilistic contingencies, relative to healthy control (see Supplementary Figure 1A). This description of the data was supported by a two-way ANOVA that revealed main effects of group [$F(1,69)=17.17$; $p<0.001$], and reward contingency [$F(2,138)=7.29$; $p<0.001$], along with a significant group x reward contingency interaction [$F(2,138)=8.15$; $p<0.001$], such that controls performed better than patients in the 80% [least-squared means $t(138)=4.66$; $p<0.001$] and 70% [$t(138)=3.61$; $p<0.001$] reward probability conditions. In the 60% condition, means for both groups were close to chance levels of performance, and did not differ [$t(138)=0.38$].

Additional post-hoc tests revealed that patients with schizophrenia showed performance that was less differentiated among the three reinforcement conditions (see Supplementary Figure 1A). In the first two blocks of the acquisition phase, controls demonstrated learning in the 80% and 70% conditions that was clearly superior to that in the 60% condition [for 80%-60% comparison, $t(138)=4.66$, $p<0.001$; for 70%-60% comparison, $t(138)=3.61$, $p<0.001$]. Patients showed no difference in performance among the three conditions, achieving less than 60% accuracy in all.

The proportion of correct responses given to studied items by subjects in the post-acquisition test phase is shown in Supplementary Figure 1B. The ANOVA for these data revealed only a main effect of group [$F(1,69)=10.44$; $p=0.002$], indicating that patients performed worse than controls in this phase of Experiment 1, regardless of reinforcement condition. Thus, Experiment 1 provides robust evidence of marked reward processing impairments in patients, but we were unable to address whether this impairment resulted from a more selective deficit in the processing of positive or negative outcomes. We did not analyze the transfer results from Experiment 1 because fully 50% of patients failed to reach criterion.

Comparison of Results from Experiments 1 and 2. In order to assess how stimulus-type influenced our experiments results, we performed ANOVAs for experimental measures, with factors of experiment and group. An ANOVA for early acquisition performance data revealed a main effect of experiment [$F(1,66)=13.06$, $p<0.001$], indicating that our entire sample of subjects performed better during the acquisition phase in Experiment 2 (which used photographs of common objects) than in Experiment 1 (which used Hiragana characters). This difference in performance was probably due to easier encoding of verbalizable stimuli in Experiment 2. The main effect of experiment for early acquisition data, however, was qualified by a significant group x experiment interaction [$F(1,66)=5.30$, $p=0.025$] which resulted from patients demonstrating greater improvement from Experiment 1 to Experiment 2 [within-group $t(66)=3.95$] than controls [$t(66)=0.41$]. This disproportionate impact of encoding ease (especially verbal) on performance in the SZ group probably reflects a more general deficit in short-term memory encoding well-documented in the literature (Cairo et al 2006; Fuller et al 2005). Both controls and patients improved their test performance from Experiment 1 to Experiment 2 [$F(1,66)$ for ME of experiment=11.08, $p=0.001$; group x experiment interaction not significant, $F(1,66)=1.98$]. Thus, probabilistic learning performance was clearly influenced by stimulus characteristics, with both subjects demonstrating improved learning with verbalizable stimuli.

Analyses of Covariance for Neuropsychological and Experimental Data. In order to determine the extent to which the variance in the performance of subjects on our experimental measures reflected individual differences in performance on more standard assessments of neurocognitive function, we performed analyses of covariance (ANCOVAs) on our experimental measures. For these ANCOVAs, we used subjects' scores on the Wechsler Test of Adult Reading (WTAR) as a covariate, along with factors of group and reinforcement probability.

Subjects' scores on the WTAR showed the strongest association with probabilistic learning scores of any standard neuropsychological measure (r=0.242; P>0.10). For the data from Experiment 1, an ANCOVA revealed that the main effect of group remained for both the early acquisition phase [F(1,67)=11.63; p=0.001] and the post-acquisition test phase [F(1,67)=6.15; p=0.016]. For the data from Experiment 2, which had shown no main effects of group, the group by reinforcement probability interactions remained significant for both the early acquisition phase [F(2,130)=3.91; p=0.022] and the post-acquisition test phase [F(2,132)=3.60; p=0.030]. Main effects of reward contingency also remained significant in the early acquisition phases of both experiments, as well as the post-acquisition test phase of Experiment 2 (F values ranged from 7.33 to 10.00). Thus, our experimental findings of impaired acquisition of probabilistic contingencies by SZ patients do not merely reflect global impairments in neurocognitive functioning common to schizophrenia.

Correlation analyses between medication doses and experimental measures. In order to assess whether performance on our experimental measures was directly attributable to the dopamine-blocking effects of antipsychotic medications, we analyzed correlations between measures of probabilistic learning and medication doses, converted to haloperidol-equivalent units. Haloperidol-equivalent doses were computed according to the guidelines of the Expert Consensus Panel for Optimizing Pharmacologic Treatment of Psychotic Disorders (2003), with doses added for patients taking multiple antipsychotic medications (see Supplementary Table 1). Where no haloperidol-equivalent dose was listed in the table for a given dose of another medication, we used linear interpolation to estimate the haloperidol-equivalent dose for a given antipsychotic dose.

We found that antipsychotic doses did not correlate significantly with mean proportion correct during early acquisition (r= -0.065), mean proportion correct for training pairs at post-acquisition test (r= -0.028), or performance on either transfer measure from the post-acquisition

test phase (r= 0.116 for “Choose A” scores; r= - 0.188 for “Avoid B” scores). Thus, performance of patients on experimental measures cannot be explained solely by treatment with antipsychotic drugs.

Figure Captions

Supp. Fig. 1. Acquisition of probabilistic contingencies by patients (SZs) and controls (NCs) in Experiment 1. (A) In blocks 1 and 2. (B) Performance on training pairs at post-acquisition test. The proportion of correct responses was defined as the proportion of trails on which the most-frequently reinforced stimulus was chosen. In both panels, black bars = control subjects, white bars = patients.

Supp. Fig. 2. Impact of trial-by-trial task feedback on subsequent choices in a given condition in first acquisition block (20 trials in each stimulus condition) of Experiment 1. "Win-stay" scores reflect the proportion of repeated stimulus selections in a given condition following reinforced choices. "Lose-shift" scores reflect the proportion of *switched* stimulus selections in a given condition following non-reinforced choices. Total "win-stay" and "lose-shift" scores were generated by averaging scores across conditions for each. Black bars = control subjects, white bars = patients.

References

Cairo TA, Woodward TS, Ngan ET (2006): Decreased encoding efficiency in schizophrenia. *Biol Psychiatry* 59:740-746.

Expert Consensus Panel for Optimizing Pharmacologic Treatment of Psychotic Disorders (2003): Expert Consensus Guideline Series: Optimizing Pharmacologic Treatment of Psychotic Disorders. *J Clin Psychiat* 64:2-97.

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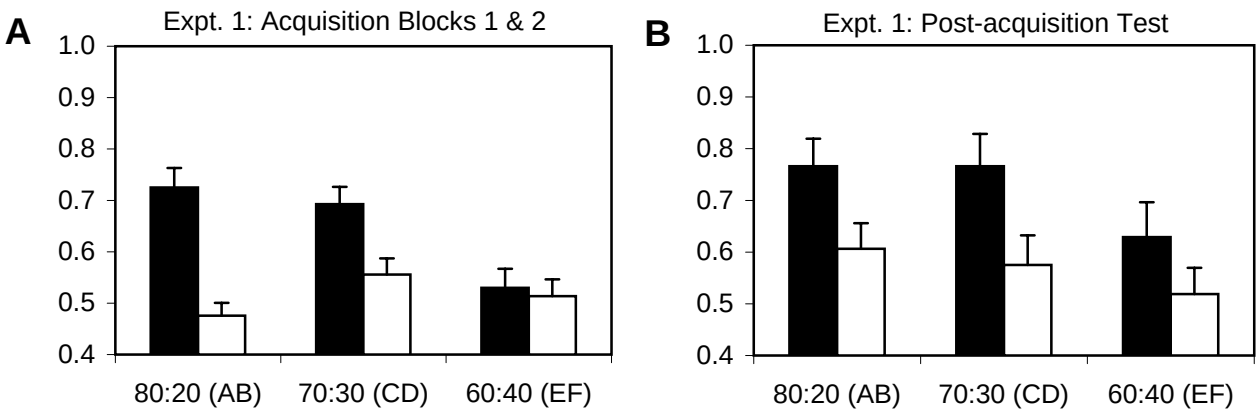
Supplementary Table 1. Patient Antipsychotic Medication Data

		First Antipsychotic Medication			Second Antipsychotic Medication		
Sub	Total HD Eq	Compound	Dose*	HD Eq	Compound	Dose*	HD Eq
1	13.0mg	Clozapine	500mg	13.0mg			
2	3.3mg	Clozapine	175mg	3.3mg			
3	2.1mg	Clozapine	125mg	2.1mg			
4	6.4mg	Clozapine	300mg	6.4mg			
5	17.0mg	Clozapine	600mg	17.0mg			
6	13.0mg	Clozapine	500mg	13.0mg			
7	4.4mg	Clozapine	225mg	4.4mg			
8	16.8mg	Clozapine	400mg	9.3mg	Risperidone	4mg	7.5mg
9	20.5mg	Clozapine	500mg	13.0mg	Risperidone	4mg	7.5mg
10	28.6mg	Clozapine	700mg	21.1mg	Risperidone	4mg	7.5mg
11	13.9mg	Clozapine	300mg	6.4mg	Risperidone	4mg	7.5mg
12	8.5mg	Clozapine	250mg	5.0mg	Risperidone	2mg	3.5mg
13	13.5mg	Clozapine	425mg	10.0mg	Risperidone	2mg	3.5mg
14	18.5mg	Clozapine	450mg	11.0mg	Risperidone	4mg	7.5mg
15	16.8mg	Clozapine	400mg	9.3mg	Risperidone	4mg	7.5mg
16	9.1mg	Clozapine	100mg	1.6mg	Risperidone	4mg	7.5mg
17	19.5mg	Clozapine	475mg	12.0mg	Risperidone	4mg	7.5mg
18	14.0mg	Clozapine	500mg	13.0mg	Quetiapine	100mg	1.0mg
19	21.4mg	Clozapine	300mg	6.4mg	Fluphen Decanoate	37.5 mg $^{Q\ 2\ weeks}$	15.0mg
20	7.5mg	Olanzapine	15mg	7.5mg			
21	23.3mg	Olanzapine	35mg	23.3mg			
22	26.7mg	Olanzapine	40mg	26.7mg			
23	7.5mg	Olanzapine	15mg	7.5mg			
24	7.5mg	Risperidone	4mg	7.5mg			
25	11.5mg	Risperidone	6mg	11.5mg			
26	7.5mg	Risperidone	4mg	7.5mg			
27	3.5mg	Risperidone	2mg	3.5mg			
28	9.5mg	Risperidone	5mg	9.5mg			
29	3.5mg	Risperidone	2mg	3.5mg			
30	4.2mg	Ziprasidone	80mg	4.2mg			
31	7.5mg	Fluphen Decanoate IM	18.75 mg $^{Q\ 2\ weeks}$	7.5mg			
32	10.0mg	Fluphen Decanoate IM	25 mg $^{Q\ 2\ weeks}$	10.0mg			
33	10.0mg	Fluphen Decanoate IM	25 mg $^{Q\ 2\ weeks}$	10.0mg			
34	12.5mg	Haloperidol	5mg	5.0mg	Halop. Decanoate IM	125 mg $^{Q\ 2\ weeks}$	7.5mg
35	5.0mg	Haloperidol	5mg	5.0mg			
36	15.0mg	Halop. Decanoate IM	125 mg $^{Q\ 2\ weeks}$	15.0mg			
37	4.0mg	Haloperidol	4mg	4.0mg			
38	2.3mg	Halop. Decanoate IM	50 mg $^{Q\ 4\ weeks}$	2.3mg			
39	7.5mg	Aripiprizole	15mg	7.5mg			
40	20.0mg	Aripiprizole	30mg	20.0mg			

*** Daily dose by mouth unless otherwise noted**

Supplemental figure 1



Reinforcement Probability for Correct: Incorrect Choice (Stimulus Pair)

Supplemental figure 2