Published in final edited form as:

Neuropsychology. 2008 September ; 22(5): 606–617. doi:10.1037/a0012602.

Impaired Implicit Learning in Schizophrenia

William P. Horan,
University of California, Los Angeles

Michael F. Green,
University of California, Los Angeles, VA Greater Los Angeles Healthcare System

Barbara J. Knowlton,
University of California, Los Angeles

Jonathan K. Wynn,
University of California, Los Angeles

Jim Mintz, and
University of Texas Health Science Center at San Antonio

Keith H. Nuechterlein
University of California, Los Angeles

Abstract

Schizophrenia patients consistently show deficits on tasks of explicit learning and memory. In contrast, their performance on implicit processing tasks often appears to be relatively intact, though most studies have focused on implicit learning of motor skills. This study evaluated implicit learning in 59 medicated schizophrenia outpatients and 43 healthy controls using two different cognitive skill tasks. Participants completed a Probabilistic Classification task to assess procedural habit learning and an Artificial Grammar task to assess incidental learning of complex rule-based knowledge, as well as an explicit verbal learning and memory task. In addition to performing worse than controls on the explicit learning task, patients showed worse overall performance on the Probabilistic Classification task, which involves gradual learning through trial-by-trial performance feedback. However, patients and controls showed similar levels of learning on the Artificial Grammar task, suggesting a preserved ability to acquire complex rule-based knowledge in the absence of performance feedback. Discussion focuses on possible explanations for schizophrenia patients' poor Probabilistic Classification task performance.

Keywords

schizophrenia; implicit learning; neurocognition; habit learning

Please address correspondence to: William P. Horan, Ph.D., 300 UCLA Medical Plaza, Suite 2240, Los Angeles, CA 90095-6968, 310.206.8181 (voice), 310.206.3651 (fax), horan@ucla.edu (e-mail).

¹Results were similar when the groups were compared on d' , a related signal detection discrimination index that accounts for incorrect detection rates, with patients ($M = .43$, $SD = .49$) not significantly differing from controls ($M = .54$, $SD = .52$), $t(98) = 1.12$, $p > .05$.

Publisher's Disclaimer: The following manuscript is the final accepted manuscript. It has not been subjected to the final copyediting, fact-checking, and proofreading required for formal publication. It is not the definitive, publisher-authenticated version. The American Psychological Association and its Council of Editors disclaim any responsibility or liabilities for errors or omissions of this manuscript version, any version derived from this manuscript by NIH, or other third parties. The published version is available at <http://www.apa.org/journals/neu>

Introduction

Schizophrenia patients consistently demonstrate substantial impairment on neurocognitive tests of explicit learning and memory (Aleman, Hijman, de Haanm, & Kahn, 1999; Heinrichs & Zakzanis, 1998), which require effortful conscious awareness during information acquisition and retrieval. These impairments have considerable functional relevance, as they are associated with how well patients function in the community and how much they benefit from psychosocial rehabilitation programs (Green, 1996; Green, 2000). In contrast, the smaller literature on implicit learning and memory in schizophrenia shows much more variability. Implicit learning refers to skill, habit, or knowledge acquisition that occurs automatically and outside of conscious awareness, whereas implicit memory refers to information retrieval that occurs outside of conscious awareness (Squire & Zola, 1996). The majority of implicit processing studies in schizophrenia have examined motor learning tasks, such as the pursuit rotor task or mirror drawing task (e.g., (Kern, Green, & Wallace, 1997; Sponheim, Steele, & McGuire, 2004; Wexler et al., 1997)). These studies tend to find intact implicit motor learning in schizophrenia, although impairments in implicit learning have been found in some studies, particularly on the serial reaction time task (e.g., (Exner, Boucsein, Degner, & Irle, 2006; Exner, 2006; Green, Kern, Williams, McGurk, & Kee, 1997; Schwartz, Howard, Howard, Hovaguimian, & Deutsch, 2003); also see (Goldberg, Saint-Cyr, & Weinberger, 1990; Gras-Vincendon et al., 1994; Michel, Danion, Grange, & Sandner, 1998)).

Implicit learning is a multi-faceted construct and it can be roughly divided into motor and cognitive learning, which appear to rely on different neural circuits (Ashby & Maddox, 2005; Keri, 2003; Yin & Knowlton, 2006). To date, implicit learning of cognitive skills has received comparatively less attention in schizophrenia research. The most extensively studied cognitive implicit learning tasks in the basic cognitive science literature involve perceptual category learning, such as the “Weather Prediction” or probabilistic classification task (PC; (Knowlton, Mangels, & Squire, 1996b)) and artificial grammar tasks (AG; (Reber, 1967)). In the PC task, participants gradually learn to predict the weather (will it “rain” or “shine”?) across a number of trials based on associations between stimuli (geometric forms) that are independently and probabilistically related to the weather outcome (rather than a deterministic, one-to-one mapping between each stimulus combination and outcome). After each trial, the subject is informed that his choice is “right” or “wrong”, but no other feedback is provided. Healthy subjects typically show significant classification improvements across learning trials but, because of the probabilistic nature of this task, are unable to explicitly state the rules that govern their predictions.

The AG task also involves category learning across a series of trials, yet differs from the PC task in several respects. In the learning stage of the task, participants are shown a series of exemplars of grammatical letter strings that are based on a complex, finite-state grammar system. In a separate testing stage of the task, subjects are asked to classify a new set of letter strings as either “grammatical” or “not-grammatical” with no feedback provided about the accuracy of their choices. Healthy subjects typically perform significantly above chance-levels in their grammaticality classifications, but are unable to explicitly state the rules that govern their responses because of the complexity of the underlying grammar system.

The PC and AG category learning tasks appear to rely on different neural circuitry. For example, successful performance on PC tasks typically does not depend on the medial temporal lobe explicit memory system (although it can under certain circumstances (e.g., (Foerde, Knowlton, & Poldrack, 2006)). Amnesic and Alzheimer’s patients with medial temporal lobe damage have typically been found to perform normally on both the PC task (e.g., (Knowlton, Mangels, & Squire, 1996a; Knowlton, Squire, & Gluck, 1994); but see (Hopkins, Myers, Shohamy, Grossman, & Gluck, 2004)) and the AG task (e.g., (Knowlton & Squire, 1996;

Reber, Martinez, & Weintraub, 2003)). In contrast, patients with Parkinson's or Huntington's disease, who exhibit abnormal striatal dopamine functioning, show impaired performance on the PC task yet preserved AG task performance (Eldridge, Masterman, & Knowlton, 2002; Knowlton, Mangels et al., 1996b; Knowlton et al., 1994; Knowlton, Squire et al., 1996; Smith, Siebert, McDowall, & Abernethy, 2001). In conjunction with human neuroimaging studies (e.g., (Lieberman, Chang, Chiao, Bookheimer, & Knowlton, 2004; Moody, Bookheimer, Vanek, & Knowlton, 2004; Poldrack, Prabhakaran, Seger, & Gabrieli, 1999; Yin & Knowlton, 2006)), these findings suggest that an intact neostriatal habit learning system is critical for PC task performance, but not for the AG task.

Only a handful of studies have examined these category learning tasks in schizophrenia. For the PC task, two studies reported that patients demonstrated worse overall percentage correct scores than healthy controls, though the slopes of the learning curves during the task did not significantly differ between groups (Keri, 2005; Weickert et al., 2002). Another study reported performance deficits only in patients taking typical antipsychotic medications, which have relatively high dopamine D₂ receptor affinities, while patients taking atypical antipsychotics did not significantly differ from controls (Beninger et al., 2003). Finally, one study reported intact performance in schizophrenia (Keri et al., 2000), but used an idiosyncratic administration procedure that makes comparison to the other studies difficult.

For the AG task, we are aware of only two studies that examined performance in schizophrenia patients. Danion and colleagues (Danion, Meulemans, Kauffmann-Muller, & Vermaat, 2001) found that schizophrenia patients and healthy controls both significantly exceeded chance-levels in their accuracy judgments and did not significantly differ from each other. A subsequent study also reported intact AG performance in a small sample of 10 schizophrenia patients (Hsieh et al., 2004).

There has been some debate among cognitive scientists about whether the learning that occurs on the AG task truly reflects deep, abstract rule-based learning, or instead reflects superficial, exemplar-specific learning. On average, grammatical test strings are likely to bear greater superficial similarity (e.g., in terms of specific bigram or trigram chunks that also occur during training trials) to the learning strings than do the nongrammatical test strings. This superficial similarity between learning and testing strings creates an interpretative confound in traditional AG tasks by providing an alternative learning strategy that does not rely on deep, rule-based knowledge.

To address this confound, researchers have used a "balanced chunk strength" design, in which grammatical and non-grammatical test strings are intentionally matched for both high and low chunk strengths (Knowlton & Squire, 1994, 1996). Chunk strength refers to the number of times bigram or trigram chunks within a test string are repeated across the training strings. This design enables investigators to directly examine whether participants' use complex, rule-based knowledge, above and beyond information about the superficial characteristics of test strings in making their grammaticality judgments. Research using this experimental design in healthy participants' indicates that although grammaticality judgments are to some extent influenced by chunk strength, they are indeed influenced by abstract rule-based knowledge as well (Chang & Knowlton, 2004; Knowlton & Squire, 1996). In the schizophrenia research literature, Danion and colleagues (Danion et al., 2001) used grammatical and non-grammatical test strings that were matched for mean levels of chunk strength. In the current study, chunk strength was manipulated as an independent variable using a balanced chunk strength design to allow us to directly evaluate whether patients use abstract, rule-based knowledge in their grammaticality judgments.

The current study examined the performance of stabilized schizophrenia outpatients and healthy controls on the PC task and the AG task, as well as measures of general verbal ability and explicit learning. By examining the performance of patients on two different implicit learning tasks, we will be able to better identify those aspects of implicit learning that may be impaired in schizophrenia. Based on existing studies, we predicted that schizophrenia patients would demonstrate worse performance than controls on the explicit learning and memory tasks and the PC task, but that the groups would show comparable levels of learning on the AG task.

Methods

Participants

Participants included 59 schizophrenia outpatients and 43 non-patient controls. Patients met criteria for schizophrenia based on the Structured Clinical Interview for DSM-IV (SCID (First, 1996)). Diagnostic interviewers were trained to a minimum Kappa of 0.75 for rating psychotic and mood symptoms by the Treatment Unit of the Veterans Integrated Service Network 22, Mental Illness Research, Education, and Clinical Center. Patients were excluded for current substance use disorders (within the past six months), but not excluded for only a history of substance use disorder. All patients were receiving various antipsychotic medications at clinically determined dosages ($n = 50$ for atypical only; $n = 3$ for typical only; $n = 6$ for both). Four patients were prescribed benzodiazepines, and these patients were asked to refrain from taking these medications on the day of testing (i.e., at least 12 hours before assessment). Nine patients were prescribed anticholinergic medications.

Nonpatient controls were recruited through newspaper advertisements and flyers posted in the local community. Controls were screened with the Structured Clinical Interview for DSM-IV for Axis I and Axis II (First, Spitzer, Gibbon, Williams, & Benjamin, 1994) and were excluded if they met criteria for any psychotic disorder, bipolar mood disorder, recurrent depression, substance dependence, or paranoid, schizotypal, schizoid, avoidant or borderline personality disorder. Controls were also excluded for current substance abuse (within the past six months), or if there was any evidence (according to participant report) of a history of psychotic disorder among their first-degree relatives. Additional exclusion criteria for all patients and controls included age less than 18 or over 55 years, identifiable neurological disorder, mental retardation, or seizure disorder.

Clinical Ratings

Brief Psychiatric Rating Scale (BPRS)—For all patients, psychiatric symptoms during the previous month were rated using the expanded 24-item UCLA version of the BPRS (Lukoff, Nuechterlein, & Ventura, 1986; Overall & Gorham, 1962) by a trained rater. Each item is rated on a scale ranging from 1 – 7. BPRS raters achieved a median intraclass correlation coefficient of .80 or higher across all items compared with the criterion ratings (Ventura, Green, Shaner, & Liberman, 1993). From this version of the BPRS, five empirically derived subscales scores (based on the mean of items comprising the scale; (Guy, 1976)) and a 24-item total score are derived.

Scale for the Assessment of Negative Symptoms (SANS)—Negative symptoms during the preceding month were evaluated using the SANS (Andreasen, 1984). Four SANS global scales were used in the current study, Affective flattening, Alogia, Anhedonia-Asociality, and Avolition-Apathy. The SANS Attention scale was not included in the current analyses given findings suggesting that this scale is not conceptually related to the negative symptom complex (e.g., (Blanchard & Cohen, 2006)).

Measures

Wechsler Test of Adult Reading (WTAR; (Wechsler, 2001))—This is a task of general word knowledge that is frequently used as an estimate of premorbid verbal ability. Participants are handed a written list of 50 words and are asked to read aloud all of the words to the best of their ability. A total score is calculated from the number of correctly pronounced words.

Hopkins Verbal Learning Test (HVLT) – Revised—In the HVLT (Benedict, Schretlen, Groninger, & Brandt, 1998; Brandt & Benedict, 2001), a list of 12 words drawn from three semantic categories is presented across three learning trials with recall assessed after each trial. After the third trial, a new list of 12 words is presented and recall assessed. Tests of cued and free recall for the first list are administered after both short and long (20 min) delays. After the long delay recall, a 24-item recognition test is administered. Dependent measures selected for the current study were the total number of correct responses for each of the three learning trials and an overall learning slope.

Probabilistic Classification Task

Procedure—This computerized task was identical to that procedure described by Knowlton et al. (1996). Participants were instructed that they would see various combinations of four different cue cards (depicting circles, diamonds, squares, or triangles) on each trial, and that their task was to decide whether each particular combination of cues they were shown predicted either “rain” or “sunshine”. Each cue card was associated with one of two outcomes (rain vs. sunshine) with a fixed probability. One, two, or three cue cards appeared on each trial and the two outcomes occurred equally often. Thus, there were 14 possible cue combinations. As shown in Table 1, the overall probability of each outcome (rain or sunshine) on a given trial was calculated according to the conditional probabilities for each of the presented cue cards.

Each participant received one of two different randomized sequences of cue combinations (Sequence A or Sequence B), that were each constructed with the constraint that the same cue card combination could not appear twice in succession and each outcome occurred no more than five times in a row. Participants were told that at first they would be guessing but that they would gradually become better at deciding which cues predicted sunshine and rain.

At the start of each trial, the cues appeared on the computer screen for 5 s. The participant indicated his or her choice by pressing either the key labeled “sunshine” or the key labeled “rain” on the computer keyboard. If the response was correct, a high-pitched tone sounded, a smiling face appeared at the right of the screen, and a vertical scoring bar at the right of the screen, initially set at 600, incremented 1 point. If the response was incorrect, a low-pitched tone sounded, a frowning face appeared at the right side of the screen, and the vertical bar at the right of the screen decremented by 1 point. Then, the icon (sun or rain) corresponding to the correct answer appeared on the screen above the cues for 2 s. If no response was made within 3 s, a prompt appeared on the screen asking for a response. After 5 s without a response, the trial was terminated, the low tone sounded, and the correct answer appeared above the cues for 2 s (these missed trials were not scored). Participants were allowed a short break (<1 min) after 50 trials. After a total of 100 trials were completed, they were administered an eight-item, four-alternative multiple-choice explicit memory task that asked about the nature of the cues and feedback, the layout of the screen, and the testing procedure (e.g., how many squares appeared on the card with squares?).

Scoring—A response was considered to be correct on a particular trial if the outcome selected was the outcome more strongly associated with the cue combination that appeared on that trial. Because of the probabilistic nature of the task, a cue combination was sometimes followed by the less strongly associated outcome. Thus, a response could be scored as correct on a particular

trial, even though the feedback indicated that the response was incorrect. In this way, the percentage correct score reflected how well participants learned the cue-outcome associations. Because the two outcomes occurred equally often, chance performance was 50% correct. The data were not analyzed for trials on which the two outcomes were equally associated with the cue combination and on which there was therefore no correct answer. These trials composed 10.7% of all the trials. Percent correct was calculated for each block of 20 trials. In addition, an overall learning slope and a total score on the explicit memory task were calculated for each subject.

Artificial grammar task

This procedure followed the exact specifications of Chang and Knowlton (2004), consisting of a training phase and a testing phase. Prior to training, participants were told that they were going to be shown a series of cards containing letter strings that they were to memorize. There was no mention of the artificial grammar rule system.

Training—Participants were presented with a series of 23 grammatical strings that was presented twice. All strings were generated from a finite-state Markovian rule system consisting only of the letters *X*, *J*, *V*, and *T*, and were thus “grammatical” (see Figure 1). Grammatical letter strings were generated by starting at the “IN” arrow and picking up a letter while traversing from one state to the next until an “OUT” arrow is reached. All letter strings varied in length from two letters to six letters, and were printed in Times font black ink in font size 100 white 5 x 8 index cards. Each index card containing one string was presented for 3 s. After each presentation, participants were asked to reproduce the string on paper. If a participant correctly reproduced the string, the next card was shown. If the participant did not correctly reproduce the string, he or she was shown the same card again for 3 s and was asked to reproduce it again. If the participant still could not reproduce the string, this process was repeated. We allowed subjects up to three trials to reproduce each string in order to ensure that all letter strings were attended during encoding. After three presentations and three attempts to reproduce the string, the experimenter moved on to present the next string.

There was a 5-min delay between the training and testing phases. In order to discourage active rehearsal of the training items, we administered the Raven Progressive Matrices Task (Raven, 1941) during the delay. This is a nonverbal reasoning task that would be unlikely to interfere with knowledge of the artificial grammar.

Testing—After the 5-min delay, participants were given the following instructions: “The orders of the letters in the previous set of cards were actually determined by a complex set of grammatical rules. You will now be presented with another set of cards for an unlimited amount of time. Your task is to decide whether each item was or was not formed according to the same rules. If the current letter string follows the same rules as the strings you were shown earlier, they should be considered ‘grammatical.’ Otherwise, they should be considered ‘not grammatical.’ Since these grammatical rules are very complex, you should base your judgments on a gut feeling as to whether each test item obeys these rules without trying to figure out the rules. Please determine if the following letter strings are ‘grammatical’ or ‘not grammatical.’”

Participants were shown a series of 32 cards, each of which had a letter string that had not been previously seen. Half of the strings were grammatical, and half were not grammatical (nongrammatical test strings were formed by introducing an error in one position to an otherwise grammatical string). The order of the strings was mixed such that no more than three items of the same chunk strength (either high or low) or grammatical status (grammatical or not grammatical) were shown in succession. Chunk strength was calculated as the average

number of times each of the bigrams and trigrams in the string had been presented in the training set (see Knowlton & Squire, 1996). As shown in Table 2, the average chunk strength of high chunk-strength items was 8.5; the average strength of low chunk-strength items was 5.6. Participants' verbal responses to the grammatical status of the letter strings were recorded by the experimenter.

Half of the test items had high chunk strengths, whereas the other half had low chunk strengths. Of the grammatical and nongrammatical test strings, there were an equal number of high chunk-strength and low chunk-strength items. From this task, an overall percent correct score was calculated, as well as the number of high chunk strength and low chunk strength items that were endorsed as "grammatical" during the testing trials.

Data analysis

Group differences in demographics were evaluated with paired t-tests for continuous variables and chi-square tests for categorical variables. Data were missing for 3 patients and 1 control on the PC task, and for 2 patients on the AG task. For the primary analyses, group differences across learning trials on the HVLT and across blocks of trials on the PC task were evaluated using separate mixed effects regression analyses. These models used total correct scores as the dependent variables, subject as a random effect to account for the non-independence of observations across trials, and group as a fixed factor. In addition, linear function terms were included as covariates to evaluate the presence of group X learning slope interactions (preliminary analyses indicated that linear effects were much stronger than quadratic effects for the learning slopes). Effect sizes for these analyses are presented as F^2 , which corresponds to the following effect size conventions: small (.02), medium, (.15) and large (.35) (Cohen, 1988). On the AG task, group differences in overall percent correct scores were evaluated with independent samples t-tests. These were followed by a 2 (group) X 2 (high chunk vs. low chunk) X 2 (grammatical vs. non-grammatical) ANOVA to evaluate the sensitivity of judgments of grammar and chunk strength. Effect sizes are presented as Cohen's partial eta squared (η_p^2), which corresponds to the following conventions: small (.01), medium, (.06) and large (.14) (Cohen, 1988). Finally, within each group, associations among measures were evaluated with Pearson correlation coefficients. Associations between performance measures and symptoms were also evaluated within the patient group.

Results

Participant characteristics and verbal ability

As shown in Table 3, the groups did not significantly differ on age, sex, education, parental education, ethnicity or marital status. This outpatient schizophrenia sample had mild to moderate levels of symptoms on the BPRS subscales and total scores that are typical for stabilized, community-dwelling samples. Mean ratings on the BPRS subscales (possible ranges 1–7) were: Anergia ($M = 1.8$, $SD = .7$), Anxiety/Depression ($M = 2.5$, $SD = .9$), Thought Disturbance ($M = 2.8$, $SD = 1.1$), and Activation ($M = 1.2$, $SD = .3$), Hostile Suspiciousness ($M = 2.1$, $SD = .7$). The mean BPRS Total score (based on the sum of the 24 BPRS items, possible range = 24–168) was 46.3 ($SD = 8.9$). Mean scores on the SANS subscales were: Affective flattening ($M = 1.9$, $SD = 1.3$), Alogia ($M = .8$, $SD = 1.0$), Apathy/Avolition ($M = 2.9$, $SD = 1.2$), and Anhedonia/Asociality ($M = 2.5$, $SD = 1.2$). Patients had a mean duration of illness of 17.4 years ($SD = 9.3$). On the WTAR, scores were significantly lower in patients ($M = 30.6$, $SD = 9.7$) than controls ($M = 35.6$, $SD = 8.8$), $t(100) = 2.70$, $p < .01$, Cohen's $d = .54$, indicating lower general verbal abilities in the patient group.

Hopkins Verbal Learning Test

Group by trial data are displayed graphically in Figure 2. A mixed-effects regression analysis indicated a significant effect for group, $F(1,100) = 5.52$, $p < .05$, $F^2 = .06$, with patients demonstrating generally lower scores than controls. There was also a linear effect for the learning slope across trials, $F(1,202) = 393.74$, $p < .001$, $F^2 = 1.95$. However, the group X slope interaction was not significant, $F(1,202) = 1.69$, $p > .05$, $F^2 = .01$, suggesting comparable learning curves across the groups.

Probabilistic Classification task

The number of no response trials was very low in both groups, with similar levels found in patients ($M = .30$, $SD = .79$) and controls ($M = .30$, $SD = .62$), $t(96) = .11$, $p > .05$, $d = .02$. Group by trial block (in blocks of 20 trials) data are displayed graphically in Figure 3. A mixed-effects regression analysis revealed significant effects for group, $F(1,96) = 7.12$, $p < .01$, $F^2 = .07$, indicating lower overall scores for patients. The learning slope across trials demonstrated a significant linear function, $F(1,390) = 47.08$, $p < .001$, $F^2 = .12$. However, the group X learning slope interaction was not significant, $F(1,390) = 1.94$, $p > .05$, $F^2 = .001$, indicating generally comparable overall learning rates in both groups. In addition, the group effect remained significant with WTAR scores entered as a covariate, $F(1,95) = 5.95$, $p < .05$, $F^2 = .06$. The magnitude of the group difference on total percent correct scores between patients ($M = .59$; $SD = .11$) and controls ($M = .65$; $SD = .14$) was medium ($d = .47$). Although the group X learning slope interaction was not statistically significant, the effect size estimates presented in Figure 3 indicate that the magnitude of the between-group differences tended to be larger during the later trial blocks of the task. A supplemental analysis of group differences within each trial block indicated that patients and controls did not significantly differ during the first two blocks, but did significantly differ during the final three blocks (p 's $< .05$).

During the first block of 20 trials, both groups performed better than would typically be expected on this task. A more detailed analysis of the data indicated that there were some performance differences during early trials depending on the trial sequence received by the participant. For Sequence A ($n = 46$), one of the cues was strongly linked to the outcome "sun" across the first 10 trials, which resulted in above chance performance for both groups in the first block of 20 trials. This earlier learning in the first 10 trials was non-significantly greater in control participants ($M = .65$, $SD = .18$) than in the patients ($M = .56$, $SD = .21$), $t(44) = 1.55$, $p > .05$, $d = .47$. In contrast, Sequence B ($n = 52$) did not appear to afford such early learning, with more typical chance-level performance shown during the first 10 trials by both controls ($M = .51$, $SD = .16$) and patients ($M = .50$, $SD = .18$). Despite these early differences in performance on the two trial sequences, the overall pattern of results was similar for participants receiving the different sequences, with no significant group X slope interactions for Sequence A or B (p 's $> .05$).

On the accompanying explicit memory task, scores were significantly lower for patients ($M = .61$, $SD = .11$) than controls ($M = .67$, $SD = .13$), $t(96) = 2.22$, $p < .05$, $d = .45$. However, scores for each group were significantly above chance-level (p 's $< .001$), suggesting adequate attentiveness to the task in both groups.

Because of the relatively high striatal D₂ receptor blockade associated with typical antipsychotic medications, supplemental analyses examined whether the above findings were attributable to patients taking these medications. There was no significant difference in total percent correct scores for patients taking typical ($n = 6$, $M = .59$, $SD = .11$) versus atypical ($n = 50$, $M = .59$; $SD = .13$) antipsychotics, $t(54) = .01$, $p > .05$, $d = .002$. We also re-ran the mixed-effects regression analysis entering only those patients who were taking atypical antipsychotics only. Fifty of the 56 patients who completed the PC task were taking only

atypical antipsychotic medications. Results were highly similar, with significant effects for group, $F(1,88) = 6.29$, $p < .05$, $F^2 = .07$ and learning slope (linear function) across trials, $F(1,358) = 51.89$, $p < .001$, $F^2 = .14$, but a non-significant interaction, $F(1,358) = .98$, $p > .05$, $F^2 = .003$, suggesting a similar pattern among patients taking only atypical antipsychotics. Finally, we re-ran the mixed-effects regression analysis entering only those patients who were not prescribed anticholinergic medications at the time of testing ($n = 47$). Again, the results were highly similar to the full analyses, with significant effects for group, $F(1,87) = 6.05$, $p < .05$, $F^2 = .07$, and linear trend, $F(1,354) = 45.29$, $p < .001$, $F^2 = .13$, but a nonsignificant group X linear trend interaction, $F(1,354) = 1.56$, $p > .05$, $F^2 = .004$, suggesting that the group differences were not solely accounted for by patients taking typical anticholinergics

Artificial Grammar task

During the learning phase, the number of learning trials required was significantly greater for patients ($M = 54.8$, $SD = 9.3$) than controls ($M = 51.3$, $SD = 4.4$), $t(98) = 2.49$, $p < .05$, $d = .50$. During the testing phase, the total percentages of correct responses were significantly above chance in both patients ($M = .56$, $SD = .10$) and controls ($M = .58$, $SD = .10$), providing evidence consistent with rule-based learning in both groups. These percentages did not significantly differ between groups, $t(98) = 1.08$, $p > .05$, $d = .22$. In addition, there were no significant differences between patients taking typical ($M = .55$, $SD = .09$) versus atypical ($M = .56$, $SD = .10$) antipsychotic medications, $t(55) = .30$, $p > .05$, $d = .08$.

During the training phase, the schizophrenia group required more learning trials than the controls, raising concerns that the patients' apparently normal performance might be attributable to higher levels of exposure to the training stimuli. We re-ran the analyses using a subset of patients ($n = 37$) who were matched to controls on total learning trials by discarding from the analyses patients who needed more presentations than the mean of the comparison subjects plus one standard deviation. Results confirmed the previous analyses, as total percent correct scores in this subset of patients ($M = .57$, $SD = .08$) did not significantly differ from controls ($p > .05$). Thus, additional exposure to training strings in a subset of patients does not appear to be the cause of the patient groups' normal performance on the AG task.

Next, using the entire sample, endorsement frequencies for specific types of test items were evaluated using a 2 (group) x 2 (grammaticality) x 2 (chunk strength) ANOVA. As displayed graphically in Figure 5, patients and controls were responsive to both grammaticality and chunk strength in their responses. There were significant main effects of grammatical status, $F(1, 98) = 64.06$, $p < .001$, $\eta_p^2 = .39$, and chunk strength, $F(1, 98) = 200.36$, $p < .001$, $\eta_p^2 = .67$, demonstrating that participants more frequently endorsed items that followed the grammatical rules and items with high chunk strengths. However, the group main effect was non-significant, $F(1,98) = 1.87$, $p > .05$, $\eta_p^2 = .02$, and there were no significant interactions between group and the other two variables (all p 's $> .05$).

Across groups, there was a significant grammaticality x chunk strength interaction, $F(1,98) = 16.46$, $p < .001$, $\eta_p^2 = .14$. Post hoc tests indicated that chunk strength exerted most of its effect on nongrammatical items. Endorsement frequencies did not significantly differ for high chunk strength-grammatical versus high chunk strength-non-grammatical items, $t(98) = .78$, $p > .05$, $d = .16$. However, endorsement frequencies were significantly higher for low chunk strength-grammatical items than for low chunk-non-grammatical items, $t(98) = 14.18$, $p < .001$, $d = 2.86$.

We re-ran this ANOVA using the subset of patients ($n = 37$) who were matched to controls on total learning trials as described above. The results were highly similar. There were significant effects for grammaticality, $F(1,78) = 48.87$, $p < .001$, $\eta_p^2 = .38$, and chunk strength, $F(1,78) = 175.85$, $p < .001$, $\eta_p^2 = .70$, as well as the grammar X chunk strength interaction, $F(1,78) =$

15.81, $p < .001$, $\eta_p^2 = .17$. However, the group effect was non-significant, $F(1,78) = .59$, $p > .05$, $\eta_p^2 = .01$, and there were no significant interactions involving group (all F 's $< .70$). Thus, patients and controls both used rule-based knowledge, above and beyond superficial chunk strength, when it came to endorsing grammatical-low chunk strength items.

Correlational analyses

As shown in Table 4, within the schizophrenia group, there were no significant correlations between verbal ability, explicit task variables, and implicit task variables. Higher learning slopes on the PC task significantly correlated with higher hostility ratings, which was not predicted and possibly a chance finding due to the number of correlations examined. Associations with symptoms were otherwise generally non-significant and small. Within the control group, there were no significant correlations among the cognitive task variables, with no correlations exceeding .25².

Discussion

Consistent with a large body of research, schizophrenia patients demonstrated explicit learning and memory impairments on tasks that involved effortful, conscious awareness at the time of knowledge acquisition and retrieval. This was evident in patients' lower scores on the HVLT, as well as their lower scores on the explicit memory test in the PC task and their need for more learning trials on the AG task. The lack of association between the explicit and implicit tasks in both groups is consistent with the theoretical distinction between explicit and implicit learning processes (Squire & Zola, 1996).

In contrast to the patients' pervasive explicit learning deficits, they demonstrated a varied pattern of performance across the cognitive implicit learning tasks. The lack of association between the PC and AG tasks in both groups is consistent with theoretical distinctions between different types of cognitive implicit learning (Ashby & Maddox, 2005; Keri, 2003). Consistent with prior studies of schizophrenia patients taking primarily atypical antipsychotics (Keri, 2005; Weickert et al., 2002), patients demonstrated an overall impairment on the PC task as compared to controls. However, they performed as well as controls on an AG task that used a balance chunk strength design, which clearly indicated that patients used deep, rule-based knowledge (in addition to superficial exemplar-based learning) to perform this task. This finding converges with prior AG studies suggesting that at least some aspects of cognitive implicit learning may be preserved in schizophrenia (Danion et al., 2001; Hsieh et al., 2004), similar to the pattern of cognitive implicit learning found in Parkinson's and Huntington's patients (Knowlton, Mangels et al., 1996a; Knowlton, Squire et al., 1996).

Although the patients demonstrated significantly worse overall performance than controls in the PC task, one might question whether the patients would achieve normal levels if they were given additional learning trials. The current results do not clearly support this possibility, as the magnitudes of the between-group differences were generally larger during the later trial blocks. In addition, a recent study of automaticity in schizophrenia by Foerde et al. (Foerde et al., in press) that included 600 PC trials does not support this possibility. In that study, schizophrenia patients and healthy controls completed twelve 50-trial blocks of the PC task (under single-task or dual task conditions) over three separate training sessions. Controls reached asymptote by the end of the first session and showed little improvement in the subsequent sessions. In contrast, patients showed only slight improvement across the three sessions and never reached the level of performance that controls reached after many more trials than were used in the current study.

²The full correlation matrix is available from the authors upon request.

Why might the schizophrenia patients have demonstrated worse performance than controls on the PC task but not on the AG task? While these tasks differ in several respects (see Smith & MacDowall, 2006), the most salient difference may be that the PC involves gradually learning to associate stimuli with behavioral responses through probabilistically-determined, trial-by-trial feedback, whereas no feedback is provided in the AG task. An interesting set of studies strongly suggests that the impaired PC performance shown by Parkinson's patients (in the context of normal AG performance) reflects impaired ability to use basal ganglia-mediated feedback to guide learning of stimulus-response associations, rather than differences in the format or complexity of these tasks. For example, Shohamy and colleagues (Shohamy, Myers, Onlaor, & Gluck, 2004) modified the PC task to eliminate the feedback aspect of the original procedure, and found that Parkinson's patients performed normally on the modified no-feedback version of the task, but worse than controls on the original version. Similarly, Smith and McDowall (2006) modified the original AG task to incorporate trial-by-trial feedback and found that Parkinson's patients demonstrated impaired performance on the modified feedback version of the task. These authors proposed that patients with pathology of the striatum differ from controls in their ability to incrementally learn complex categorization rules based on trial-by-trial feedback. This explanation is consistent with evidence that dopaminergic transmission in the basal ganglia plays a crucial role in reinforcement learning and reward-based decision-making by generating reward prediction errors (Frank & Claus, 2006; Packard & Knowlton, 2002; Schultz, Dayan, & Montague, 1997). In line with these findings, Parkinson's patients show abnormal Error Related Negativity (Falkenstein, 2001), an electrophysiological index of error monitoring.

One speculative, post hoc explanation for the current findings is that schizophrenia patients' poor PC performance reflects impaired feedback-based learning, perhaps associated with striatal pathology. Striatal pathology may be a core pathophysiological feature of this disorder (Chatterjee et al., 1995; Corson, Nopoulos, Andreasen, Heckel, & Arndt, 1999; Gur et al., 1998). We previously found abnormal reward processing in schizophrenia using the Iowa Gambling task, a category learning task that depends on different types of reward or punishment feedback (Shurman, Horan, & Nuechterlein, 2005). In addition, schizophrenia patients have shown abnormal Error Related Negativity (Morris, Yee, & Nuechterlein, 2006) and, in fMRI studies, decreased striatal activation during reward processing (Juckel et al., 2006) and motor implicit learning (Reiss, in press). The hypothesis of impaired feedback-based implicit learning in schizophrenia could be directly evaluated in future research by administering feedback and non-feedback versions of the PC and AG tasks (e.g., Shohamy et al. 2004; Smith & McDowall 2006). Further research on basal ganglia-mediated reward processing could also help illuminate the mechanisms of schizophrenia patients' learning difficulties and possibly certain clinical features, such as anhedonia (Horan, Blanchard, & Kring, 2006).

Several other factors could account for the patients' poor performance on the PC task. One factor is the psychometric properties of the implicit learning tasks. Chapman and Chapman (1983; 1978) described the importance of developing cognitive tasks that are matched for reliability, difficulty, and variance levels when evaluating possible differential ability deficits in clinical populations. The implicit learning tasks selected for use in this study were not specifically designed to demonstrate a differential deficit, and they differed on these characteristics. The PC task demonstrated a split-half reliability coefficient of .81 and a mean difficulty level (proportion correct) of .65 ($SD = .14$), whereas the AG task demonstrated a split-half reliability coefficient of .60 and a mean difficulty level of .58 ($SD = .09$). In addition, differences in the formats of the tasks make direct comparisons difficult. For example, the PC task is about three times as long as the AG task, possibly contributing to its better reliability. Another key difference is that learning occurs gradually throughout the testing phase of the PC task whereas the AG task is comprised of separate training and testing phases. Given these task

differences, we cannot definitively conclude from the current study that patients showed a differential deficit on the PC task.

Another factor to consider is potential medication effects. Although impairment on the PC task in the schizophrenia group was not directly attributable to patients who were taking conventional antipsychotics, the atypical medications that most patients were taking do, to varying extents, affect striatal dopamine transmission (Abi-Dargham & Laurelle, 2005), which could have impacted their performance (Beninger et al., 2003). Alternative research strategies, such as studying unmedicated and recent-onset patients, or studying patients who were randomly assigned to different types of medications, could help to address this possible explanation.

Alternatively, as suggested by Weickert and colleagues (2002), the patients' PC impairment could reflect disturbances in other aspects of neurocognition, rather than deficient cognitive implicit learning per se. For example, it has been proposed that the medial temporal lobe and associated explicit learning functions may interact (or compete) with the basal ganglia during the early stages of performing this task (Poldrack & Rodriguez, 2004). Furthermore, performance can be improved on this task even in patients with striatal pathology by recruiting medial temporal lobe regions (Moody et al., 2004). Indeed, college undergraduates appear to be able to rely on medial temporal lobe regions in this task unless they are learning under cognitive load (Foerde et al., 2006). Although this study did not include a comprehensive neuropsychological assessment battery, the lack of correlation between PC task and HVLT performance observed here argues against a contribution of explicit processing deficits to poor performance on the PC task in this study. Along these lines, it may be informative for later studies to conduct a fine-grained analysis of the characteristic learning strategy that individuals with schizophrenia use to perform the PC task, as has been done in studies of amnesic patients (Gluck, Shohamy, & Myers, 2002; Meeter, Myers, Shohamy, Hopkins, & Gluck, 2006).

The divergent pattern of implicit learning shown by individuals with schizophrenia may be useful for developing theoretical models of the mechanisms through which neurocognitive deficits impact daily life functioning and for guiding clinical interventions. Many social cognitive processes that are required for adaptive social functioning appear to be learned and enacted automatically (Bargh & Williams, 2006; Lieberman, 2000; Satpute & Lieberman, 2006). As noted by Danion and colleagues (2001), intact aspects of implicit learning during development and everyday life may help explain why, despite pervasive explicit processing deficits, patients' functional capacities are generally not grossly impaired. However, when automatic processing is guided by emotional contingencies, as is often the case in the social environment, disturbed aspects of implicit learning could contribute to patients' social functioning difficulties (Bargh & Williams, 2006). In future research, it will be useful to determine whether performance on implicit learning tasks correlate with measures of social cognition or actual community functioning in schizophrenia.

In terms of clinical implications, schizophrenia patients' ability to implicitly learn through repeated exposure without trial-by-trial feedback on the AG task appears to be a relative strength that psychosocial rehabilitation can capitalize on. For example, compensatory training techniques such as errorless learning, which minimizes the use of feedback to correct past mistakes and guide subsequent behavior, have proven useful in helping schizophrenia patients develop specific vocational skills and even social problem solving skills (Kern et al., 2005; Kern, Liberman, Kopelowicz, Mintz, & Green, 2002). It remains to be determined whether the type of learning difficulty shown by patients on the PC task is amenable to restorative rehabilitation approaches.

Acknowledgements

This research was supported by a NARSAD Young Investigator Award (William P. Horan, Ph.D.), by research grants MH43292 and MH65707 (P.I.: Michael F. Green, Ph.D.) and Institutional NRSA MH14584 (P.I.: Keith H. Nuechterlein, Ph.D.) from the National Institute of Mental Health, and by the Department of Veterans Affairs VISN 22 Mental Illness Research Education and Clinical Center. We thank Shelly M. Crosby, Teena D. Moody, Kelly Tillery, Joseph Ventura, and Sarah Wilson for their contributions to this project.

References

- Abi-Dargham A, Laurelle M. Mechanisms of action of second generation antipsychotic drugs in schizophrenia: insights from brain imaging studies. *European Psychiatry* 2005;20:15–27. [PubMed: 15642439]
- Aleman A, Hijman R, de Haanm EHF, Kahn RS. Memory impairment in schizophrenia: A meta-analysis. *American Journal of Psychiatry* 1999;256(9):1358–1366. [PubMed: 10484945]
- Andreasen, NC. The Scale for the Assessment of Negative Symptoms (SANS). Iowa City, IA: The University of Iowa; 1984.
- Ashby FG, Maddox WT. Human category learning. *Annual Review of Psychology* 2005;56:149–178.
- Bargh JA, Williams EL. The automaticity of social life. *Current Directions in Psychological Science* 2006;15:1–4. [PubMed: 18568084]
- Benedict RHB, Schretlen D, Groninger L, Brandt J. Hopkins Verbal Learning Test–Revised: Normative data and analysis of inter-form and test-retest reliability. *Clinical Neuropsychologist* 1998;12:43–55.
- Beninger RJ, Wasserman J, Zanibbi K, Charbonneau D, Mangels J, Beninger BV. Typical and atypical antipsychotic medications differentially affect two nondeclarative memory tasks in schizophrenic patients: a double dissociation. *Schizophrenia Research* 2003;61:281–292. [PubMed: 12729880]
- Blanchard JJ, Cohen AS. The structure of negative symptoms within schizophrenia: implications for assessment. *Schizophr Bull* 2006;32(2):238–245. [PubMed: 16254064]
- Brandt, J.; Benedict, RJB. The Hopkins Verbal Learning Test- Revised: Professional Manual. Odessa: Psychological Assessment Resources, Inc.; 2001.
- Chang GY, Knowlton BJ. Visual feature learning in artificial grammar classification. *Journal of Experimental Psychology: Learning, Memory, & Cognition* 2004;30(3):714–722.
- Chapman JP, Chapman LJ. Reliability and the discrimination of normal and pathological groups. *Journal of Nervous and Mental Disease* 1983;171:546–661. [PubMed: 6886683]
- Chapman LJ, Chapman JP. The measurement of differential deficit. *Journal of Psychiatric Research* 1978;14:303–311. [PubMed: 722633]
- Chatterjee A, Chakos M, Koren A, Geisler S, Sheitman B, Woerner M, Kane JM, Alvir J, Lieberman JA. Prevalence and clinical correlates of extrapyramidal signs and spontaneous dyskinesia in never-medicated schizophrenic patients. *American Journal of Psychiatry* 1995;152:1724–1729. [PubMed: 8526237]
- Cohen, J. *Statistical Power Analysis for the Behavioral Sciences*. 2. Hillsdale, NJ: Erlbaum; 1988.
- Corson PW, Nopoulos P, Andreasen NC, Heckel D, Arndt S. Caudate size in first-episode neuroleptic-naïve schizophrenic patients measured using an artificial neural network. *Biological Psychiatry* 1999;46:712–720. [PubMed: 10472424]
- Danion JM, Meulemans T, Kauffmann-Muller F, Vermaat H. Intact implicit learning in schizophrenia. *American Journal of Psychiatry* 2001;158(6):944–948. [PubMed: 11384904]
- Eldridge LL, Masterman D, Knowlton BJ. Intact implicit habit learning in Alzheimer's disease. *Behavioral Neuroscience* 2002;116(4):722–726. [PubMed: 12148939]
- Exner C, Boucsein K, Degner D, Irle E. State-dependent implicit learning deficit in schizophrenia: evidence from 20-month follow-up. *Psychiatry Research* 2006;142(1):39–52. [PubMed: 16580734]
- Exner C, Weniger G, Schmidt-Samoa C, Irle E. Reduced size of the pre-supplementary motor cortex and impaired motor sequence learning in first-episode schizophrenia. *Schizophrenia Research* 2006;84:386–396. [PubMed: 16624528]

- Falkenstein M, Hielcher H, Dziobek I, Schwarzenau P, Hoormann J, Sunderman B, Hohnsbein J. Action monitoring, error detection, and the basal ganglia: an ERP study. *NeuroReport* 2001;12:157–161. [PubMed: 11201078]
- First, MB.; Gibbon, M.; Spitzer, RL.; Williams, JBW. Structured Clinical Interview for DSM-IV Axis I Disorders. Patient Edition. New York: Biometrics Research; 1996.
- First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW.; Benjamin, L. Structured Clinical Interview for DSM-IV Axis II Personality Disorders (Version 2.0). New York, NY.: New York State Psychiatric Institute; 1994.
- Foerde K, Knowlton BJ, Poldrack RA. Modulation of competing memory systems by distraction. *Proceedings of the National Academy of Sciences* 2006;103:11778–11783.
- Foerde K, Poldrack RA, Knowlton BJ, Sabb FW, Bookheimer SY, Bilder RM, Guthrie D, Granholm E, Nuechterlein KH, Marder SR, Asarnow RF. Selective corticostriatal dysfunction in schizophrenia: Examination of motor and cognitive skill learning. *Neuropsychology*. in press
- Frank MJ, Claus ED. Anatomy of a decision: Striato-orbitofrontal interactions in reinforcement learning, decision making, and reversal. *Psychological Review* 2006;113:300–206. [PubMed: 16637763]
- Gluck MA, Shohamy D, Myers C. How do people solve the “weather prediction” task? Individual variability in strategies for probabilistic category learning. *Learning and Memory* 2002;9:408–418. [PubMed: 12464701]
- Goldberg TE, Saint-Cyr JA, Weinberger DR. Assessment of procedural learning and problem solving in schizophrenic patients by Tower of Hanoi type tasks. *J Neuropsychiatry Clin Neurosci* 1990;2(2): 165–173. [PubMed: 2136071]
- Gras-Vincendon A, Danion JM, Grange D, Bilik M, Willard-Schroeder D, Sichel JP, Singer L. Explicit memory, repetition priming and cognitive skill learning in schizophrenia. *Schizophr Res* 1994;13(2): 117–126. [PubMed: 7986768]
- Green MF. What are the functional consequences of neurocognitive deficits in schizophrenia? *American Journal of Psychiatry* 1996;153(3):321–330. [PubMed: 8610818]
- Green MF, Kern RS, Williams O, McGurk S, Kee K. Procedural learning in schizophrenia: Evidence from serial reaction time. *Cognitive Neuropsychiatry* 1997;2(2):123–134.
- Green MF, Kern RS, Braff DL, Mintz J. Neurocognitive deficits and functional outcome in schizophrenia: Are we measuring the “right stuff”? *Schizophrenia Bulletin* 2000;26(1):119–136. [PubMed: 10755673]
- Gur RE, Maany V, Mozley PD, Swanson C, Bilker W, Gur RC. Subcortical MRI volumes in neuroleptic-naïve and treated patients with schizophrenia. *American Journal of Psychiatry* 1998;155:1711–1717. [PubMed: 9842780]
- Guy, W. ECDEU Assessment Manual for Psychopharmacology. Rockville, MD: U.S. Department of Health, Education, and Welfare; 1976.
- Heinrichs RW, Zakzanis KK. Neurocognitive deficit in schizophrenia: A quantitative review of the evidence. *Neuropsychology* 1998;12:426–445. [PubMed: 9673998]
- Hopkins R, Myers C, Shohamy D, Grossman S, Gluck M. Impaired probabilistic category learning in hypoxic subjects with hippocampal damage. *Neuropsychologia* 2004;42:524–535. [PubMed: 14728924]
- Horan WP, Blanchard JJ, Kring AM. Anhedonia in schizophrenia: A review of assessment strategies. *Schizophrenia Bulletin* 2006;32(2):359–373.
- Hsieh MH, Liu K, Liu SK, Chiu MJ, Hwu HG, Chen AC. Memory impairment and auditory evoked potential gating deficit in schizophrenia. *Psychiatry Research* 2004;130(2):161–169. [PubMed: 15033186]
- Juckel G, Schlagenhauf F, Koslowski M, Wustenberg T, Villringer A, Knutson B, Wrase J, Heinz A. Dysfunction of ventral striatal reward prediction in schizophrenia. *Neuroimage* 2006;29:409–416. [PubMed: 16139525]
- Keri S. The cognitive neuroscience of category learning. *Brain Research Reviews* 2003;43:85–109. [PubMed: 14499464]
- Keri S, Juhasz A, Rimanoczy A, Szekeres G, Kelemen O, Cimmer C, Szendi I, Benedek G, Janka Z. Habit learning and the genetics of the dopamine D3 receptor: evidence from patients with

- schizophrenia and healthy controls. *Behavioral Neuroscience* 2005;119(3):687–693. [PubMed: 15998189]
- Keri S, Kelemen O, Szekeres G, Bagoczky N, Erdelyi R, Antal A, Benedek G, Janka Z. Schizophrenics know more than they can tell: probabilistic classification learning in schizophrenia. *Psychological Medicine* 2000;30:149–155. [PubMed: 10722185]
- Kern RS, Green MF, Mitchell S, Kopelowicz AJ, Mintz J, Liberman RP. Extensions of errorless learning for social problem-solving deficits in schizophrenia. *American Journal of Psychiatry* 2005;162:513–519. [PubMed: 15741468]
- Kern RS, Green MF, Wallace CJ. Declarative and procedural learning in schizophrenia: a test of the integrity of divergent memory systems. *Cognitive Neuropsychiatry* 1997;2:39–50.
- Kern RS, Liberman RP, Kopelowicz A, Mintz J, Green MF. Applications of errorless learning for improving work performance in persons with schizophrenia. *American Journal of Psychiatry* 2002;159:1921–1926. [PubMed: 12411229]
- Knowlton BJ, Mangels JA, Squire LR. A neostriatal habit learning system in humans. *Science* 1996a; 273:1399–1402. [PubMed: 8703077]
- Knowlton BJ, Mangels JA, Squire LR. A neostriatal habit learning system in humans. *Science* 1996b; 273(5280):1399–1402. [PubMed: 8703077]
- Knowlton BJ, Squire LR. The information acquired during artificial grammar learning. *Journal of Experimental Psychology: Learning, Memory, & Cognition* 1994;20(1):79–91.
- Knowlton BJ, Squire LR. Artificial grammar learning depends on implicit acquisition of both abstract and exemplar-specific information. *Journal of Experimental Psychology: Learning, Memory, & Cognition* 1996;22(1):169–181.
- Knowlton BJ, Squire LR, Gluck M. Probabilistic classification learning in amnesia. *Learning and Memory* 1994;1(2):106–120. [PubMed: 10467589]
- Knowlton BJ, Squire LR, Gluck M, Paulsen JS, Swerdlow NR, Swenson M. Dissociations within nondeclarative memory in Huntington's disease. *Neuropsychology* 1996;10(4):538–548.
- Lieberman MD. Intuition: A social cognitive neuroscience approach. *Psychological Bulletin* 2000;126:109–137. [PubMed: 10668352]
- Lieberman MD, Chang GY, Chiao J, Bookheimer SY, Knowlton BJ. An event-related fMRI study of artificial grammar learning in a balanced chunk strength design. *Journal of Cognitive Neuroscience* 2004;16(3):427–438. [PubMed: 15072678]
- Lukoff D, Nuechterlein KH, Ventura J. Manual for the expanded Brief Psychiatric Rating Scale. *Schizophrenia Bulletin* 1986;12:578–602. [PubMed: 3810065]
- Meeter M, Myers CE, Shohamy D, Hopkins RO, Gluck MA. Strategies in probabilistic categorization: Results from a new way of analyzing performance. *Learning and Memory* 2006;13:230–239. [PubMed: 16547162]
- Michel L, Danion JM, Grange D, Sandner G. Cognitive skill learning and schizophrenia: implications for cognitive remediation. *Neuropsychology* 1998;12(4):590–599. [PubMed: 9805329]
- Moody TD, Bookheimer SY, Vanek Z, Knowlton BJ. An implicit learning task activates medial temporal lobe in patients with Parkinson's disease. *Behavioral Neuroscience* 2004;118(2):438–442. [PubMed: 15113271]
- Morris SE, Yee CM, Nuechterlein KH. Electrophysiological Analysis of Error Monitoring in Schizophrenia. *Journal of Abnormal Psychology* 2006;115:239–250. [PubMed: 16737389]
- Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. *Psychological Reports* 1962;10:799–812.
- Packard MG, Knowlton BJ. Learning and memory functions of the Basal Ganglia. *Annual Review of Neuroscience* 2002;25:563–593.
- Poldrack RA, Prabhakaran V, Seger CA, Gabrieli JDE. Striatal activation during acquisition of a cognitive skill. *Neuropsychology* 1999;13:564–574. [PubMed: 10527065]
- Poldrack RA, Rodriguez P. How do memory systems interact? Evidence from human classification learning. *Neurobiology of Learning and Memory* 2004;82:324–332. [PubMed: 15464413]
- Reber AS. Implicit learning of artificial grammars. *Journal of Verbal Learning and Verbal Behavior* 1967;6:855–863.

- Reber PJ, Martinez LA, Weintraub S. Artificial grammar learning in Alzheimer's disease. *Cognitive & Affective Behavioral Neuroscience* 2003;3(2):145–153.
- Reiss JP, Campbell DW, Leslie WD, Paulus MD, Ryner LN, Polimeni JO, Foot BJ, Sareen J. Deficit in schizophrenia to recruit the striatum in implicit learning: A functional magnetic resonance imaging investigation. *Schizophrenia Research*. in press
- Satpute AB, Lieberman MD. Integrating automatic and controlled processes into neurocognitive models of social cognition. *Brain Research* 2006;1079:86–97. [PubMed: 16490183]
- Schultz W, Dayan P, Montague RA. A neural substrate of prediction and reward. *Science* 1997;275:1593–1599. [PubMed: 9054347]
- Schwartz BL, Howard DV, Howard JH, Hovaguimian A, Deutsch SI. Implicit learning of visuospatial sequences in schizophrenia. *Neuropsychology* 2003;17(3):517–533. [PubMed: 12959517]
- Sergi MJ, Green MF. Social perception and early visual processing in schizophrenia. *Schizophrenia Research* 2002;59:233–241. [PubMed: 12414080]
- Sergi MJ, Rasseovsky Y, Nuechterlein KH, Green MF. Social perception as a mediator of the influence of early visual processing on functional status in schizophrenia. *American Journal of Psychiatry* 2006;163:448–454. [PubMed: 16513866]
- Shohamy D, Myers CE, Onlaor S, Gluck MA. Role of the basal ganglia in category learning: how do patients with Parkinson's disease learn? *Behavioral Neuroscience* 2004;118(4):676–686. [PubMed: 15301595]
- Shurman B, Horan WP, Nuechterlein KH. Schizophrenia patients demonstrate a distinctive pattern of decision-making impairment on the Iowa Gambling Task. *Schizophrenia Research* 2005;72(2–3): 215–224. [PubMed: 15560966]
- Smith J, Siegert RJ, McDowall J, Abernethy D. Preserved implicit learning on both the serial reaction time task and artificial grammar in patients with Parkinson's disease. *Brain & Cognition* 2001;45(3): 378–391. [PubMed: 11305880]
- Sponheim SR, Steele VR, McGuire KA. Verbal memory processes in schizophrenia patients and biological relatives of schizophrenia patients: intact implicit memory, impaired explicit recollection. *Schizophrenia Research* 2004;71(2–3):339–348. [PubMed: 15474904]
- Squire LR, Zola SM. Structure and function of declarative and nondeclarative memory systems. *Proceedings of the National Academy of Sciences* 1996;93:13515–13522.
- Ventura J, Green MF, Shaner A, Liberman RP. Training and quality assurance with the Brief Psychiatric Rating Scale: 'The Drift Busters'. *International Journal of Methods in Psychiatric Research* 1993;3:221–224.
- Wechsler, D. Wechsler Test of Adult Reading. London: Psychological Corporation; 2001.
- Weickert TW, Terrazas A, Bigelow LB, Malley JD, Hyde T, Egan MF, Weinberger DR, Goldberg TE. Habit and skill learning in schizophrenia: evidence of normal striatal processing with abnormal cortical input. *Learning and Memory* 2002;9(6):430–442. [PubMed: 12464703]
- Wexler BE, Hawkins KA, Rounsaville B, Anderson M, Sernyak MJ, Green MF. Normal neurocognitive performance after extended practice in patients with schizophrenia. *Schizophrenia Research* 1997;1997:173–180. [PubMed: 9323348]
- Yin HH, Knowlton BJ. The role of the basal ganglia in habit formation. *Nature Reviews Neuroscience* 2006;7(6):464–476.

Figure 1. Finite-state Markovian rule system used to generate grammatical letter strings (from Abrams & Reber, 1989). S1-S5 indicate the five possible states that occur during generation of grammatical letter strings.

Figure 2. Hopkins Verbal Learning Test performance in the schizophrenia and control groups. Error bars represent standard errors. d = standardized effect size for between-group difference.

Figure 3.

Weather Prediction Task performance in the schizophrenia and control groups. Error bars represent standard errors. d = standardized effect size for between-group difference. * = t-test for between group difference is statistically significant ($p < .05$).

Figure 4. Percentage of letter strings endorsed as grammatical in the schizophrenia and control groups. Error bars represent standard errors.

Table 1
Probability Structure of the Weather Prediction Task

Cue pattern	Cue				<i>P</i> (cue combination appearing)	<i>P</i> (feedback indicating Outcome 1 is correct)	Outcome predicted by structure
	1	2	3	4			
1	0	0	0	1	.133	.15	2
2	0	0	1	0	.087	.385	2
3	0	0	1	1	.080	.083	2
4	0	1	0	0	.087	.615	1
5	0	1	0	1	.067	.200	1
6	0	1	1	0	.04	.500	Neither
7	0	1	1	1	.047	.143	2
8	1	0	0	0	.133	.850	1
9	1	0	0	1	.067	.500	Neither
10	1	0	1	0	.067	.800	1
11	1	0	1	1	.033	.400	2
12	1	1	0	0	.08	.917	1
13	1	1	0	1	.033	.600	1
14	1	1	1	0	.047	.857	1

Note. On any trial, 1 of 14 possible combinations of four cues appeared with the probability indicated above [*P*(cue combination appearing)]. Each cue was associated with one of the two weather outcomes (1 = Sunshine vs. 2 = Rain) with a fixed probability. Across all 14 combinations of cues, Cue 1 was associated 75% of the time with Outcome 1 and 25% of the time with Outcome 2; Cue 2 was associated 56% of the time with Outcome 1 and 44% of the time with Outcome 2; Cue 3 was associated 44% of the time with Outcome 1 and 56% of the time with Outcome 2; Cue 4 was associated 25% of the time with Outcome 1 and 75% of the time with Outcome 2. Each combination of cues predicted Outcome 1 (Sunshine) with the probability shown above [*P*(feedback indicating Outcome 1 is correct)] and predicted Outcome 2 (Rain) with a probability of 1 – *P*.

Table 2
Artificial Grammar Task Test Items and Chunk Strengths (CS)

Grammatical, high chunk Strength	CS	Grammatical, low chunk strength	CS	Nongrammatical, high chunk strength	CS	Nongrammatical, low chunk strength	CS
XXVXJ	10.3	VJTVT	6.0	VJTV	7.0	XXJJ	6.8
XVTV	6.8	VTVJJ	5.1	XXV	12.0	VXJTV	4.9
VXJ	9.3	VTVJ	5.6	XVXV	10.0	XXVVJJ	6.1
XXVTV	7.9	XVJTVT	6.7	XXVJ	9.1	JXVT	5.0
XXJTVX	7.4	VTV	5.0	XXVJJJ	7.7	XXTX	2.8
XXVTVJ	7.6	XVTVJ	6.7	XJJ	7.0	TVJ	6.7
VJTXVX	6.8	XVTVJJ	6.1	VXVJ	8.2	VXJXX	5.9
VX	12.0	VTVJJJ	5.2	XVXT	7.0	VJJXVT	4.9
Mean	8.5		5.8		8.5		5.4

Table 3
Demographic Characteristics for Schizophrenia ($n = 59$) and Control ($n = 43$) Groups

Characteristic	Schizophrenia	Control	Statistic
Age (M , [SD])			
M	40.0	40.0	$t(100) = .04$
SD	11.0	9.1	
Sex			$\chi^2(1, N = 102) = .05$
Male %	76	74	
Female %	24	24	
Ethnicity			$\chi^2(1, N = 102) = 2.81$
Caucasian %	33	43	
African American %	32	35	
Hispanic %	23	15	
Asian %	7	3	
Other %	5	5	
Education (years)			$t(100) = .11$
M	14.0	13.3	
SD	2.5	2.0	
Marital status			$\chi^2(1, N = 102) = 2.45$
Never married %	67	65	
Currently married %	7	16	
Ever married %	46	43	

Table 4
Correlations Within the Schizophrenia Group ($n = 59$)

Scale	1	2	3	4
1. WTAR	-			
2. HVL: slope	.02	-		
3. PC: task slope	.04	.16	-	
4. AG task: percent correct	.17	-.04	.12	-
5. BPRS: Thought disturbance	.05	.30	.08	.25
6. BPRS: Anxiety/Depression	.06	.21	-.01	.28
7. BPRS: Anergia	.30	-.16	.08*	.29
8. BPRS: Hostility	-.11	.12	.33*	-.09
9. BPRS: Activation	.10	.32	.08	.13
10. BPRS: Total	.23	.15	.08	.30
11. SANS: Affective flattening	.12	.02	.05	.02
12. SANS: Alogia	.19	.12	.15	.01
13. SANS: Avolition/Apathy	-.14	-.02	-.17	.04
14. SANS: Anhedonia/Asociality	-.23	-.03	.06	.10

Notes: WTAR: Wechsler Test of Adult Reading; HVL: Hopkins Verbal Learning Test; PC: Probabilistic Classification; AG: Artificial Grammar; BPRS: Brief Psychiatric Rating Scale; SANS: Scale for the Assessment of Negative Symptoms.

* $p < .05$.