

Implicit Learning of Visuospatial Sequences in Schizophrenia

Barbara L. Schwartz
Washington, DC, Veterans Affairs Medical Center and
Georgetown University

Darlene V. Howard
Georgetown University

James H. Howard Jr.
The Catholic University of America

Alexandra Hovaguimian
Washington, DC, Veterans Affairs Medical Center

Stephen I. Deutsch
Washington, DC, Veterans Affairs Medical Center and Georgetown University

The authors examined whether patients with schizophrenia learned sequential patterns in a probabilistic serial response time task in which pattern trials alternated with random ones. Patients showed faster and more accurate responses to pattern trials than to random trials, but controls showed greater sensitivity to patterns. The highest level of regularity learned in both groups was information about runs of 3 events. Pattern learning occurred largely outside of awareness, as participants could not describe patterns. Controls with higher memory spans learned the sequential pattern better than those with lower memory spans, suggesting that working memory influences implicit pattern learning. Pathology in motor sequencing systems and poor working memory may lead to deficits in learning sequence structure in schizophrenia.

In everyday experience, people can learn about their surroundings without intending to do so and without being able to articulate what they have learned. One such example is how people acquire intuitive knowledge of grammatical and syntactic rules of language. Knowledge of linguistic rules is expressed by correct usage, but few people are able to verbalize many of these rules. Cognitive psychologists use the term *implicit learning* to describe the way in which people acquire intuitive knowledge about the structural relationships between events in the environment (Frensch, 1998; A. S. Reber, 1989). This type of learning is distinguished from declarative or explicit learning, in which peo-

ple deliberately apply knowledge of rules to solve problems and remember events. Under declarative conditions, people are aware of what they have learned.

People with schizophrenia have marked disturbances on declarative tests of recall and recognition that require conscious recollection of past events (Aleman, Hijman, de Haan, & Kahn, 1999; Calev, 1984; Heinrichs & Zakzanis, 1998; McKenna et al., 1990; Saykin et al., 1991). In contrast, there are recent reports that implicit learning is preserved in people with schizophrenia. In one study, normal learning was observed in an artificial grammar task (Danion, Meulemans, Kauffmann-Muller, & Vermaat, 2001). Participants in this study memorized letter strings that, unknown to the participants, conformed to the rules of a finite grammar. Artificial grammar learning was revealed by accurate classification of grammatical and ungrammatical letter strings, and the patients' classification performance did not differ from that of healthy controls (see also Abrams & Reber, 1988). In another study, patients with schizophrenia showed intact implicit learning in a probabilistic classification task in which they learned subtle covariations between cues and responses in a task of weather prediction (Kéri et al., 2000). The findings of these two recent studies bear some similarity to the findings of intact implicit processes in patients with schizophrenia in tasks that measure repetition priming and skill learning (e.g., Clare, McKenna, Mortimer, & Baddeley, 1993; Gras-Vincendon et al., 1994; Kern, Green, & Wallace, 1997; Schwartz, Rosse, & Deutsch, 1993). Collectively, these data indicate the possibility that individuals with schizophrenia perform normally on tasks that do not require conscious recollection of past events.

One exception to this fairly uniform picture is that people with schizophrenia are impaired in acquiring implicit knowledge of sequential regularities (Green, Kern, Wil-

Barbara L. Schwartz and Stephen I. Deutsch, Mental Health Service Line, Washington, DC, Veterans Affairs Medical Center, and Department of Psychiatry, Georgetown University; Darlene V. Howard, Department of Psychology, Georgetown University; James H. Howard Jr., Department of Psychology, The Catholic University of America; Alexandra Hovaguimian, Mental Health Service Line, Washington, DC, Veterans Affairs Medical Center.

This research was supported by a grant from the National Alliance for Research on Schizophrenia and Affective Disorders (NARSAD). We gratefully acknowledge Marcia Simon Kaplan for her support of this research in the NARSAD Research Partners Program. We thank Cherie Marvel and Amy Drapalski for conducting psychiatric interviews and for their helpful comments on this work. Preliminary reports of these findings were presented at the British Psychological Society meeting, Glasgow, Scotland, April 2001, and the Biological Psychiatry meeting, Philadelphia, Pennsylvania, May 2002.

Correspondence concerning this article should be addressed to Barbara L. Schwartz, Mental Health Service Line (116A), Veterans Affairs Medical Center, 50 Irving Street, Northwest, Washington, DC 20422. E-mail: Barbara.Schwartz@med.va.gov

liams, McGurk, & Kee, 1997; Kumari et al., 2002). Implicit sequence learning is most commonly studied in a version of the Serial Response Time Test introduced by Nissen and Bullemer (1987). In this task, participants see a target that appears in one of four spatial locations and press a key that corresponds to one of these locations. The target follows a fixed pattern over several blocks of trials, but participants are not informed about the repeating pattern. Sequence learning is observed when people respond faster on blocks of pattern trials than on a single block of trials in which the target follows no pattern. Although sequence learning is revealed by these objective measures, participants are often unable to describe the pattern.

The present research was designed to characterize implicit learning of sequential patterns in schizophrenia by use of a new test, the Alternating Serial Response Time (ASRT) Test (Feeney, Howard, & Howard, 2002; D. V. Howard & Howard, 2001; J. H. Howard & Howard, 1997). In this test, as in the original version, people press a key that corresponds to one of four spatial locations. The novel feature of the ASRT Test is that every other (alternate) stimulus follows a fixed pattern, and the remaining stimuli are selected randomly from one of the four spatial locations. The alternating pattern is repeated over several sessions across days. Pattern learning in the ASRT Test can be measured at any point in training by comparing the accuracy and response times between pattern and random trials. Learning in the ASRT Test is usually indicated by a divergence of pattern and random trials with practice across sessions.

The ASRT Test permits us to address issues of implicit learning in schizophrenia that could not be investigated with the original version of the Serial Response Time Test. One obstacle to overcome in studying implicit sequence learning in patients with schizophrenia is providing enough exposure to the pattern so that it is learned without providing so much exposure that people discover and memorize the pattern. Indeed, results of studies show that declarative knowledge of the pattern, or simply knowledge that the stimuli are sequenced, leads to improved performance in the Serial Response Time Test (e.g., Curran & Keele, 1993; Frensch & Miner, 1994; Willingham, Nissen, & Bullemer, 1989). It is possible that earlier findings of deficits in sequence learning in schizophrenia were attributable to control participants, but not patients, becoming aware of the sequence. This situation might have given control participants the added benefit of the use of explicit strategies as well as implicit ones. The ASRT Test is well suited to the study of implicit learning in schizophrenia patients because people are presented with over 10,000 trials containing subtle patterns but do not gain declarative knowledge of the patterns (D. V. Howard & Howard, 2001; J. H. Howard & Howard, 1997). This critical feature allows investigators to provide schizophrenia patients with ample exposure to the sequence of events in this test while still preventing explicit knowledge from occurring. We expect that, given this extensive exposure, schizophrenia patients will demonstrate pattern learning.

A second advantage of the ASRT Test is that we can examine whether or not schizophrenia patients learn about

the probabilistic nature of sequenced events. Sequences in the ASRT Test are probabilistic in that predictable elements of the pattern are embedded within random or unpredictable events. Early versions of the Serial Response Time Test were constructed so that people might have learned about the frequency of single events or pairs of events. For example, Green et al. (1997) used the 10-trial sequence DBCACBDCBA, where ABCD refers to the first, second, third, and fourth horizontal locations across the screen. Participants in this study might have learned that certain events (e.g., B) occurred with greater frequency than others in the sequence. The ASRT Test assesses knowledge about the relative frequencies of more complex sequences of events: The lowest level of structure that can be learned is a three-trial event or *triplet* (e.g., 1, R, 2). The test also provides information about whether people learn longer sequences of events. These characteristics allow us to explore whether deficits in sequence learning in schizophrenia relate to the complexity of the underlying structure of sequences.

Another advantage of the ASRT Test is that, unlike earlier studies of schizophrenia in which pattern learning could not be assessed until a random block was inserted, pattern learning can be compared between groups throughout the task by contrasting pattern and random trials in every block. In this way, we can identify the point at which responses to pattern trials diverge from those to random trials, permitting determination of whether schizophrenia patients have a slower rate of pattern learning than control participants.

From a theoretical perspective, the ASRT Test measures neurocognitive functions that are impaired in schizophrenia. These functions include the ability to actively maintain contextual information for current processing demands, retrieve events in temporal and spatial sequences, and select task-relevant stimuli while filtering task-irrelevant (random) stimuli. These cognitive processes are usually evaluated in schizophrenia by use of declarative measures (e.g., Braver, Barch, & Cohen, 1999; Elvevag, Weinberger, & Goldberg, 2001; Rizzo, Danion, Van Der Linden, Grangé, & Rohmer, 1996; Schwartz, Deutsch, Cohen, Warden, & Deutsch, 1991; Sullivan, Shear, Zipursky, Sagar, & Pfefferbaum, 1997). The ASRT Test provides a model for studying these functions in schizophrenia patients under conditions of implicit learning, so that it can be ascertained whether or not deficits are related to conscious declarative processes.

Another relevant issue for studying sequence learning in schizophrenia is the role of attention in implicit learning. Patients with schizophrenia have attention and working memory impairments that may interfere with the learning of subtle patterns in sequential response time tasks. The majority of studies that have examined the influence of attention on sequence learning have used a secondary task (e.g., tone counting) to reduce the amount of cognitive resources available for learning the sequence. These studies have led to some mixed findings. In Nissen and Bullemer's (1987) study, performance in the Serial Response Time Test was disrupted by a secondary task, but later studies suggested that the effects of attention on learning depended on the

sequence structure (Cohen, Ivry, & Keele, 1990; Curran & Keele, 1993). Other researchers found that secondary tasks, such as tone counting, affected only the expression of learning in the Serial Response Time Test and not the learning itself (Frensch, Lin, & Buchner, 1998). Jiménez and Méndez (1999) also examined the effects of selective attention on sequence learning. In their study, a second regularity was introduced so that the shape of the target predicted the spatial location on the next trial. Participants learned the sequential relationship between shapes and spatial locations only when they attended and responded to the shapes. Jiménez and Méndez (1999) suggested that attending to the predictive stimulus (shape) maintains its representation long enough so that an association with the following event can be formed. This activity likely depends on maintaining contextual information in working memory. In the study described here, we examined the relationship between sequence learning and working memory function.

We asked six main questions in this study. First, can schizophrenia patients acquire knowledge of complex sequential patterns in the ASRT Test? Second, are patients impaired on a Serial Response Time Test that provides ample opportunity for learning without the development of declarative knowledge of the pattern? Third, can patients show learning for patterns of the same structural complexity (e.g., triplets) as control participants do? Fourth, can patients and control participants express their knowledge about the sequential structure of items in a subsequent generation task that provides no feedback? Fifth, what is the role of working memory in the acquisition of sequential patterns in the ASRT Test? The sixth and final question is whether there is a correlation between the clinical features of schizophrenia (e.g., symptoms, movement disorders, and medication effects) and performance on the ASRT Test.

Method

Participants

Twenty-four patients and 24 nonpsychiatric control participants were enrolled in the study. Table 1 shows characteristics for the two groups. All participants provided informed consent prior to their participation in the study, and all were paid for their participation.

The patients were recruited from the inpatient and outpatient services in psychiatry at the Washington, DC, Veterans Affairs Medical Center. All but one patient took part in a diagnostic interview with the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID; First, Spitzer, Gibbon, & Williams, 1997). The SCID interview was administered to each patient by a trained psychiatrist, psychologist, or research technician. The diagnoses were established in consensus by at least two raters present at the SCID interview (including the interviewer), as well as by chart review and consultation with the patient's treating psychiatrist. The diagnosis for the patient who refused the SCID interview was made on the basis of a semistructured interview with the patient's psychiatrist and a review of the patient's chart. Of the 24 patients, 17 met *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; American Psychiatric Association, 1994) criteria for schizophrenia with the following subtypes: paranoid ($n = 8$),

Table 1
Characteristics of Patient and Control Groups

Characteristic	Patient	Control
Sample size	24	24
Sex ratio (male:female)	21:3	21:3
Handedness (right:left)	22:2	22:2
Ethnicity	16 African American, 8 Caucasian	23 African American, 1 Caucasian
Age (years)	42.96 (6.51)	40.42 (7.90)
Education (years)	13.06 (2.02)	13.25 (1.73)
National Adult Reading Test score	94.68 (9.03)	103.06 (7.47)
Letter-Number Sequencing Test score	6.92 (2.30)	9.71 (2.34)
Computation Span Test ^a score		
Simple span	1.5 (1.22)	2.92 (1.84)
Total span	7.19 (11.03)	20.00 (21.33)

Note. Data are reported as means (*SDs*) unless otherwise indicated.

^a Data were missing for 3 patients ($N = 21$).

undifferentiated ($n = 6$), disorganized ($n = 2$), and residual ($n = 1$). The remaining 7 patients met criteria for schizoaffective disorder.

All 24 patients were administered the Positive and Negative Syndrome Scale (PANSS; Kay, Opler, & Fiszbein, 1992) to assess the severity of their psychiatric symptoms. The rating for each item on the PANSS was determined in consensus by raters with established reliability ($k = .83$). The mean total PANSS score for the group was 72.88 ($SD = 14.19$). The mean subscale scores were 19.63 ($SD = 5.98$) for the positive scale, 18.63 ($SD = 5.77$) for the negative scale, and 34.63 ($SD = 7.63$) for the general psychopathology scale. The average duration of illness for these patients was 18.46 years ($SD = 8.47$ years).

At the time of cognitive testing, 23 of the 24 patients were being treated with antipsychotic medication: atypical ($n = 14$), typical ($n = 3$), or both types of medication ($n = 6$). The mean dose of antipsychotic medication in chlorpromazine equivalents was 955.21 mg ($SD = 824.92$ mg). Thirteen patients were also being treated with an antiparkinsonian medication (bentropine). Scores for the Abnormal Involuntary Movement Scale (AIMS; National Institute of Mental Health, 1976) were available from the patients' medical records; the scale was administered by the patient's treating physician. The average length of time between the AIMS assessment and cognitive testing for these patients was 4.7 months (range: 0–12 months). Patients were screened for medical and neurological conditions. Any patient with a diagnosis of alcohol or substance abuse within the preceding 6 months was excluded from participation in the study.

The control participants were recruited from the hospital staff and the local community. The control participants did not differ from the patients in terms of age, $t(46) = 1.22, p > .05$, or years of education completed, $t(46) = -0.35, p > .05$. The average score on the revised National Adult Reading Test (NART; Blair & Spreen, 1989) for the control participants was higher than that for the patients, $t(46) = -3.50, p < .01$. Control participants were excluded if they had a current medical, neurological, or psychiatric condition or if they had a history of psychiatric illness.

Design

The design was a $2 \times 2 \times 6$ (Group \times Trial Type \times Session) mixed factorial with group (control and patient) as a between-subjects variable and trial type (pattern and random) and session (1–6) as within-subject variables.

Stimuli and Apparatus

The ASRT Test was performed by use of an Apple computer, keyboard, and monitor. To perform the test, participants used four keys on the keyboard. They placed the index and middle fingers of their right hand on the period and question mark keys and the index and middle fingers of their left hand on the *x* and *z* keys. Four open circles were evenly spaced across the center of the screen on the computer monitor. Participants were informed that each circle corresponded to one of the four response keys. For example, the circle on the far left of the screen corresponded to the finger on the far left key. On each trial, one circle was darkened and remained darkened until the participant pressed the key that corresponded to that circle. If an incorrect key was pressed, the circle remained darkened until the correct key was pressed. There was a 120-ms delay after the key was pressed in response to the target before the next stimulus appeared on the screen.

In the ASRT Test, there is an eight-trial sequence. Every other (alternate) stimulus in the sequence follows a predetermined pattern, and the remaining stimuli are selected randomly from one of the four spatial locations on the screen. Six sequences were used: 1R2R3R4R, 1R2R4R3R, 1R3R2R4R, 1R3R4R2R, 1R4R2R3R, and 1R4R3R2R. In the sequence 1R3R2R4R, 1 refers to the leftmost position on the screen, 4 refers to the rightmost position on the screen, and R refers to a randomly selected position.

Procedure

Participants sat in front of the computer. They were told, "In this study, we are trying to learn more about how practice affects motor performance. We want to find out just how much people are able to speed their responses when they are given extended practice on a simple reaction time task." Participants were not informed that the stimuli would follow a predetermined pattern. They were instructed to respond to the stimuli as quickly as possible while maintaining a high level of accuracy, about 92% correct. Both accuracy and response time for each trial were recorded.

Participants performed the ASRT Test twice daily on three consecutive days, once in the morning and once in the afternoon, for a total of six sessions. Each session was divided into 21 blocks of 90 trials. The first 10 trials of each block were random trials. The remaining 80 trials consisted of the eight-item sequence (e.g., 1R2R3R4R) shown 10 times in a block. Therefore, the eight-trial sequence was shown 210 times in a session and 1,260 times over the six sessions. After each block of trials in a session, the participants' mean reaction time and accuracy were shown on the screen. If their accuracy was above 90%, they were encouraged to speed their responses to the targets. If their accuracy was below 90%, they were requested to slow their responses and try to concentrate on responding more accurately. Participants were required to take breaks after the completion of a block of trials to minimize fatigue. At the end of the final block for Sessions 1 through 5 participants were asked the following questions:

1. Did you use any strategy to try to improve your performance (speed or accuracy)? If so, what was your strategy?
2. Do you think your strategy worked? Why or why not?

3. Any other comments?

At the end of the sixth and final session, participants were asked the following questions:

1. Do you have anything to report regarding the task?
2. Did you notice anything special about the task or the material?
3. Did you notice any regularity in the way the stimulus was moving on the screen? (If the participant answered yes, the experimenter asked for specific details and then asked Question 4.)
4. Did you attempt to take advantage of the regularities you noticed in order to anticipate subsequent targets? If so, did this help?

After participants were asked the above questions at the end of Session 6, they performed a free generation task. In this task, participants were instructed to produce on their own a sequence of responses that resembled a sequence they experienced during the previous task. Participants responded by pressing the four response keys. The circles on the screen darkened in response to the participant's key presses, but no feedback about the accuracy of the responses was given. There was no time limit for the generation task, but participants were instructed not to deliberate on their choices, just to perform the task on the basis of their intuition. Two blocks of 80 trials each for practice were followed by four blocks of 80 trials each. Following the generation task, participants were asked the following questions:

1. Do you have anything to report regarding your experience with this task?
2. Were you able to remember a typical sequence or do you feel you were forced to guess?
3. Were you able to remember any portions of a typical sequence? (If so, please describe.)
4. Any other comments?

Working Memory Tests

Two tests were used to assess working memory. The first was the Letter–Number Sequencing Test, which is a subtest of the Wechsler Adult Intelligence Scale—Third edition (Wechsler, 1997). In this test, the experimenter read aloud a list of letters and single digits in a mixed order. The participants were instructed to first recall the numbers in ascending order and then to recall the letters in alphabetical order. The Letter–Number Sequencing Test was administered at the end of Session 5 after the completion of the ASRT Test questionnaire.

The second test of working memory was a Computation Span Test modeled after that of Salthouse and Babcock (1991). Participants were shown a simple addition problem (e.g., $6 + 2 = ?$) on the computer screen. They typed in the sum of the two digits by using the keyboard and were instructed to remember the second digit in the problem (e.g., 2). There were three trials in each of the seven span lengths ranging from 1 to 7. For an item to be scored as correct, participants had to both produce sums and recall the second digit. Two scores were obtained from the Computation Span Test by use of the scoring method of Raz, Gunning-Dixon, Head, Dupuis, and Acker (1998). The simple span was calculated

for the three trials in each span length. A score of 1 was assigned if participants responded correctly on two or three trials, and a score of .5 was assigned if they responded correctly on only one trial. The total span was the total number of correct trials across all span lengths. The Computation Span Test was administered at the end of Session 1 after the completion of the ASRT Test questionnaire.

Results

Data Analysis

Median response times for correct responses were calculated separately for pattern trials and random trials in each block (40 pattern and 40 random trials). Mean response times for pattern trials and random trials were calculated for each session by averaging across the median response times for the 21 blocks within a session. The same calculation was used to obtain the mean proportions correct for pattern trials and random trials in each session. The alpha level for all statistical tests reported here was .05, unless otherwise stated.

Did Schizophrenia Patients Learn About Sequential Patterns?

Figure 1 shows the mean proportions of correct responses for pattern and random trials in each session for the schizophrenia patients and control participants. Accuracy in pattern trials for both groups remained high over the six sessions, whereas accuracy in random trials decreased over the sessions. These results are characteristic of the results of all previous studies with the ASRT Test and reflect increasing knowledge of the regularity (Feeney et al., 2002; J. H. Howard & Howard, 1997, 2001). A 2 (group) \times 2 (trial type) \times 6 (session) analysis of variance on these data yielded a significant main effect for trial type, $F(1, 46) = 104.36, p < .01$, revealing that participants responded more accurately to pattern trials than to random trials. This finding demonstrated learning of sequential patterns in the ASRT Test. The significant two-way interaction of Trial Type \times Session, $F(5, 230) = 14.11, p < .01$, showed that the difference between pattern trials and random trials increased with practice over the six sessions. Importantly, the absence of a significant main effect for group showed that overall accuracy did not differ for the two groups. To ensure that schizophrenia patients showed pattern learning, a 2 (trial type) \times 6 (session) analysis of variance was performed on accuracy data for this group alone. Evidence of pattern learning was confirmed by a significant main effect of trial type, $F(1, 23) = 23.63, p < .01$.

The means of the median response times for pattern trials and random trials in each session are plotted in Figure 2. A 2 (group) \times 2 (trial type) \times 6 (session) analysis of variance yielded significant main effects for group, $F(1, 46) = 33.17, p < .01$, trial type, $F(1, 46) = 126.76, p < .01$, and session, $F(5, 230) = 59.42, p < .01$, and a significant interaction of Trial Type \times Session, $F(5, 230) = 7.96, p < .01$. These

results revealed that participants responded faster to pattern trials than to random trials over the six sessions. As anticipated, the patients' response times were slower than those of the control participants. Once again, an analysis performed on data for the patient group alone showed a reliable trial type effect, $F(1, 23) = 27.36, p < .01$, providing evidence of pattern learning for the patients.

Are Schizophrenia Patients Impaired in Learning of Sequential Patterns?

Although schizophrenia patients demonstrated learning in the ASRT Test, they did not show the same degree of learning as the control participants did. This finding is evident in Figures 1 and 2, where a smaller difference between pattern trials and random trials was seen for schizophrenia patients than for control participants. A 2 (group) \times 2 (trial type) \times 6 (session) analysis of variance on accuracy data showed a significant interaction of Group \times Trial Type, $F(1, 46) = 10.21, p < .01$, and a significant interaction of Group \times Trial Type \times Session, $F(5, 230) = 6.07, p < .01$. A 2 (group) \times 2 (trial type) \times 6 (session) analysis of variance on response time data showed a significant interaction of Group \times Trial Type, $F(1, 46) = 14.69, p < .01$, and a significant interaction of Group \times Trial Type \times Session, $F(5, 230) = 3.56, p < .01$. Thus, both accuracy and response time measures revealed a deficit in pattern learning for the schizophrenia patients.¹

Although the groups were matched on a number of variables, the average NART score for the patient group was significantly lower than that for the control group. In order to rule out the possibility that pattern learning was impaired in schizophrenia because these patients had lower premorbid abilities, we compared ASRT Test performances for two subgroups whose NART scores were comparable to one another. To accomplish this match, we removed 6 controls with the highest NART scores and 6 patients with the lowest NART scores. The NART scores for the remaining 18 patients ($M = 98.2, SD = 7.28$) did not differ from the NART scores for the remaining 18 controls ($M = 99.9, SD = 5.12$), $t(34) = -0.81, p > .05$. Analyses performed

¹ Additional analyses were performed to determine whether trial type effects (difference between pattern trials and random trials) in the ASRT Test were attributable to artifacts that could selectively influence random trials (Remillard & Clark, 2001). Two types of triplets occur only on random trials: repetitions (e.g., 1, 1, 1) and trills (e.g., 1, 2, 1). Previous work showed that learning in the ASRT Test is unchanged when these triplets are excluded from the analyses (D. V. Howard et al., in press). A reanalysis of our data showed that the accuracy data were unchanged. For the response time data, trial type effects were also unchanged; however, the two- and three-way interactions did not reach statistical significance. The lack of significance might have been attributable to reduced power when triplet trials were removed from the analyses.

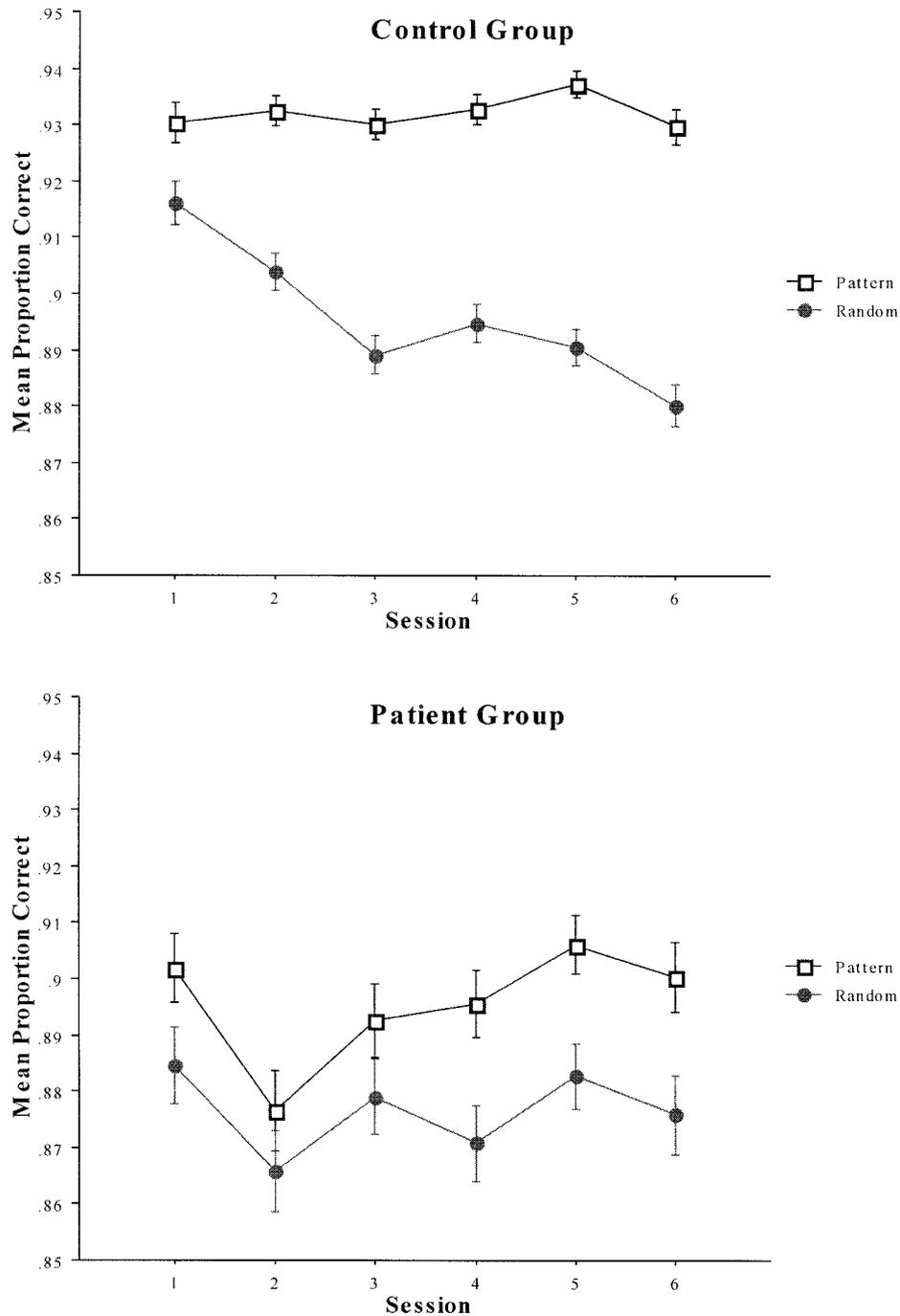


Figure 1. Mean proportions correct for pattern and random trials as a function of session for control and patient groups. Error bars of $\pm 1 SE$ are plotted.

on the accuracy and response time data for these new groups revealed the same patterns of results as for the entire group. A 2 (group) \times 2 (trial type) \times 6 (session) analysis of variance on accuracy data showed a significant main effect of trial type, $F(1, 34) = 108.95, p < .01$; significant two-way interactions of Trial Type \times Session, $F(5, 170) = 12.16, p < .01$, and Group \times Trial Type, $F(1, 34) = 12.85,$

$p < .01$; and a significant three-way interaction of Group \times Trial Type \times Session, $F(5, 170) = 4.98, p < .01$. As observed previously, overall accuracy did not differ for the groups. A 2 (group) \times 2 (trial type) \times 6 (session) analysis of variance on response time data yielded significant main effects of group, $F(1, 34) = 23.60, p < .01$, trial type, $F(1, 34) = 126.38, p < .01$, and session, $F(5, 170) = 53.87, p <$

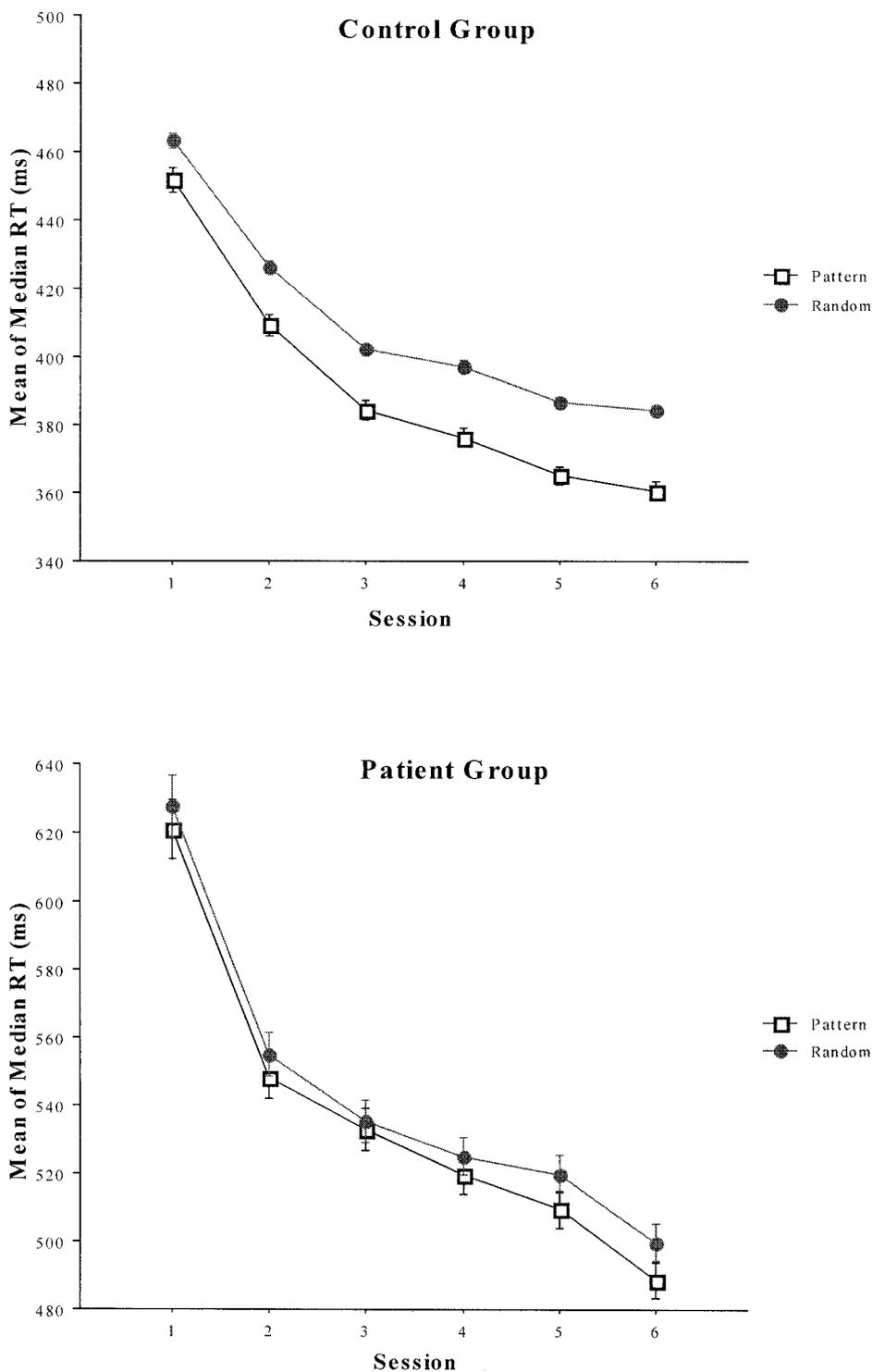


Figure 2. Means of median response times (RTs) for pattern and random trials as a function of session for control and patient groups. Error bars of $\pm 1 SE$ are plotted.

.01; significant two-way interactions of Trial Type \times Session, $F(5, 170) = 7.30, p < .01$, and Group \times Trial Type, $F(1,34) = 16.76, p < .01$; and a significant three-way interaction of Group \times Trial Type \times Session, $F(5, 170) =$

2.78, $p < .05$. These results indicated that the deficit in learning of sequential patterns in schizophrenia patients could not be attributed to a difference in estimated premorbid IQs between the two groups.

What Type of Pattern Was Learned, and Did Schizophrenia Patients Learn Something Different From What Control Participants Learned?

One possibility for why schizophrenia patients are impaired in pattern learning is that they are unable to learn about the relative frequencies of more complex sequences. The structure of the sequence in the ASRT Test permits an examination of whether participants acquire knowledge about triplets (e.g., 1, R, 2) or about sequences that are longer than triplets (e.g., 1, R, 2, R, 3). To examine this question, we separated the random trials into two types: random trials that ended in triplets that were consistent with the pattern (*random consistent*) and random trials that ended in triplets that were not consistent with the pattern (*random inconsistent*). Consider the eight-trial sequence 1R2R3R4R. The triplet 1, 2, 2 (1, R, 2; when the third item is a pattern trial) is a pattern triplet. The triplet 1, 2, 2 can also occur when the third item is a random trial (e.g., R, 2, R). Therefore, this triplet is a random-consistent triplet. In contrast, some triplets can occur only when the third item in the triplet is a random trial, never when it is a pattern trial. For example, the triplets 1, 2, 1 and 3, 2, 2 are random-inconsistent triplets because they can only occur when the third item of the triplet is a random trial (e.g., R, 2, R).

If performance on random trials for random-consistent triplets does not differ from performance on pattern trials, then this would suggest that the highest level of structure that participants learn is triplets. If, on the other hand, performance on pattern trials becomes more accurate and faster with practice than performance on random trials for random-consistent triplets, then participants must be learning sequences longer than triplets (e.g., 1, R, 2, R, 3).

The mean proportions correct for pattern trials and random trials for random-consistent triplets are plotted in Figure 3 for patients and control participants, and the corresponding data for the means of the median response times are shown in Figure 4. Performance on random trials for random-inconsistent triplets is also shown on the graphs for comparison, but these data are not relevant to the present question and therefore are not included in the analyses. The results for the accuracy and response time analyses make similar points. The highest level of structure learned consisted of three-trial events or triplets, and this was the case for both patients and control participants. A 2 (group) \times 2 (trial type: pattern, random consistent) \times 6 (session) analysis of variance on the accuracy data yielded no significant effects. A 2 (group) \times 2 (trial type: pattern, random consistent) \times 6 (session) analysis of variance on the response time data showed significant main effects of group, $F(1, 46) = 37.83, p < .01$, and session, $F(5, 230) = 73.80, p < .01$. These results showed that the response times of the patients were slower than those of the control participants and that the response times for both groups became faster with practice over sessions. However, most importantly, no main effects or interactions involving trial type (pattern vs. random consistent) were significant. These results indicated

that neither group was distinguishing between these two triplet types and, hence, that triplets were the highest level of regularity being learned.

Can Participants Express Knowledge of Sequential Patterns in a Generation Task, and Is There a Difference Between Schizophrenia Patients and Control Participants in the Expression of This Knowledge?

The generation task was analyzed by dividing trials into two types of triplets: triplets that were pattern consistent and those that were pattern inconsistent. Pattern-consistent triplets occurred frequently during the sessions given the structure of the pattern trials, whereas pattern-inconsistent triplets occurred infrequently. In the eight-trial sequence 1R2R3R4, pattern-consistent triplets for the triplet 1, r, 2 were as follows: 1, 1, 2; 1, 2, 2; 1, 3, 2; and 1, 4, 2. A triplet that was pattern inconsistent in this eight-trial sequence was 2, 1, 4, because this triplet occurred only with random events (e.g., R, 1, R). There were 16 pattern-consistent triplets and 48 pattern-inconsistent triplets for each eight-trial sequence (total number of possible triplets, 64). Therefore, the probability of generating a pattern-consistent triplet simply by chance was .25 (16/64), and the probability of generating a pattern-inconsistent triplet by chance was .75 (48/64).

In the generation task, participants performed four blocks of 80 trials each. There were 78 possible triplets in each block, or a total of 312 triplets (78 triplets \times 4 blocks). Of the 312 triplets, 78 pattern-consistent triplets would occur by chance (.25 \times 312). The question was whether or not significantly more than 78 pattern-consistent triplets would occur across the four blocks. Data were not available for analysis for 9 of the 24 control participants, so their analysis was based on 15 people. The mean frequency of occurrence of pattern-consistent triplets for control participants was 88.92, or .285 (88.92/312 = .285). The mean frequency of occurrence of pattern-consistent triplets for patients was 85.49, or .274 (85.49/312 = .274). At first glance, it is apparent that participants generated strikingly few pattern-consistent triplets. To determine whether pattern-consistent triplets were produced with a probability of greater than chance, we conducted a one-sample *t* test using a hypothesized mean of .25. The results did not reach significance for either patients, $t(23) = 1.99, p = .06$, or control participants, $t(14) = 2.06, p = .06$, but would have been significant in a one-tailed *t* test. Importantly, a comparison of the mean probabilities of producing pattern-consistent triplets between the two groups did not show a significant difference, $t(37) = 0.543, p > .05$.

Were Participants Able to Describe the Sequence?

At the end of each session, people were asked questions about their experience with the task and whether they noticed and could describe any regularity in the way in which the target moved from one spatial location to another. Re-

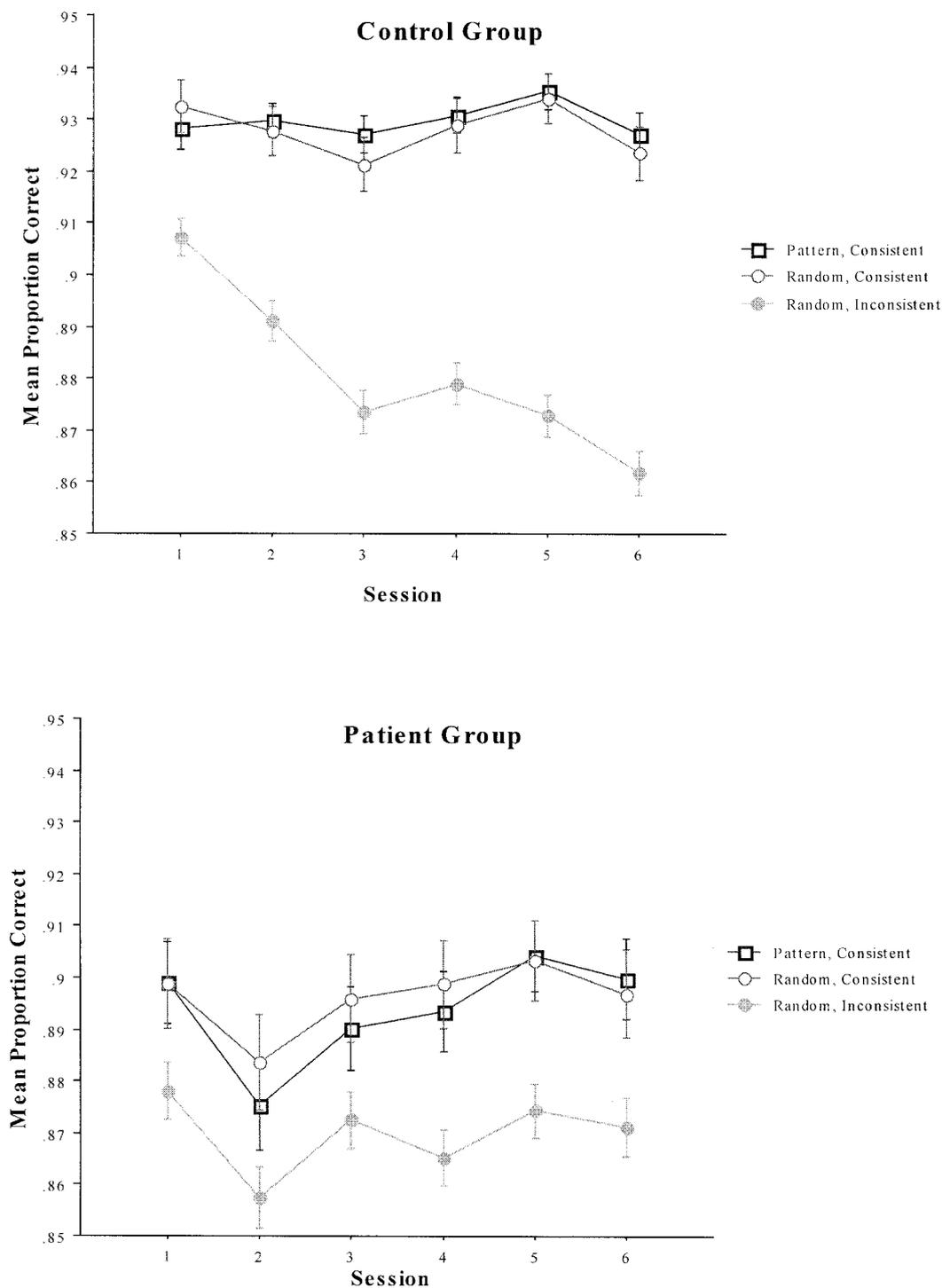


Figure 3. Mean proportions correct for pattern trials and random trials, with random trials divided into random-consistent and random-inconsistent triplets, for control and patient groups as a function of session. Error bars of ± 1 SE are plotted.

sponses to these questions were usually negative (no regularity noticed) or described haphazard movements of the target (e.g., moved from far right to far left and back to far left; target was repeated in the same position; target se-

quence changed from block to block). Certainly in no case did anyone describe a pattern in which predictable events alternated with random ones. Nor did any participant report that some triplets were more frequent than others. These

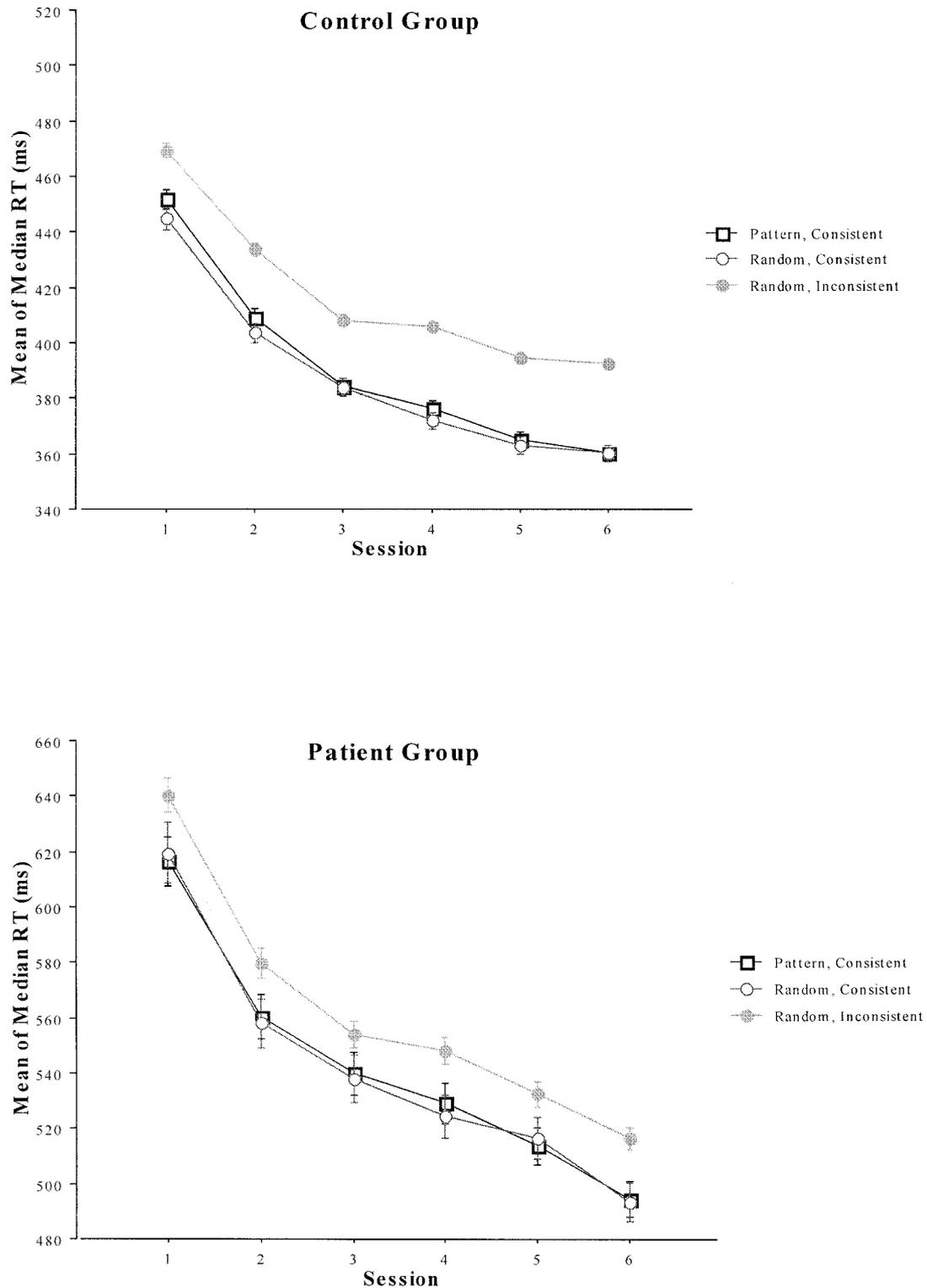


Figure 4. Means of median response times (RTs) for pattern trials and random trials, with random trials divided into random-consistent and random-inconsistent triplets, for control and patient groups as a function of session. Error bars of $\pm 1 SE$ are plotted.

results suggested that patients and control participants did not have declarative knowledge of the repeating pattern.

What Is the Role of Working Memory in Learning of Sequential Patterns?

As expected, patients were impaired on the working memory tests compared with control participants. They recalled fewer items in the Letter–Number Sequencing Test, $t(46) = -4.14, p < .01$, and had shorter memory spans with measures of both simple span, $t(43) = -2.99, p < .01$, and total span, $t(43) = -2.48, p < .05$. Total span scores were used in correlation analyses to provide a larger range of scores.

We were interested in examining the role of working memory in two components of the ASRT Test. The first component was performance, in the form of overall accuracy and overall response time, during the first session. This component measures people’s initial ability to perform the ASRT Test and reflects to some extent preexisting individual differences in performance. The second component was overall pattern learning, measured by the difference between pattern trials and random trials in Session 6. We assumed that pattern learning would be at its greatest after maximum exposure to the pattern on this final session. Correlations were determined for the data for each group separately. Data for the Computation Span Test were unavailable for 3 patients.

Working memory was related to the speed of responses in Session 1. Patients with higher span scores responded faster to random trials, $r = -.50, p < .05$, and pattern trials, $r = -.49, p < .05$. Likewise, patients who recalled more items in the Letter–Number Sequencing Test responded faster to random trials, $r = -.41, p < .05$, and pattern trials, $r = -.41, p < .05$. Similar patterns were observed for control participants in Session 1. Span scores were correlated to median response times for random trials, $r = -.44, p < .05$, and pattern trials, $r = -.42, p < .05$. The correlation between Letter–Number Sequencing Test scores and median response times reached only trend levels for control participants, $r = -.40, p = .06$, for pattern trials, and $r = -.35, p = .09$, for random trials. These data indicated that people with higher working memory scores responded faster to targets during the early phase of training in the ASRT Test. It is possible that working memory influenced performance at a time when people were becoming familiar with the correspondence between spatial locations and response keys. During this phase, there may have been a fine-tuning of visuomotor processing in which performance was under strategic control, with greater demands on working memory.

There was also evidence that working memory played a role in pattern learning. We did not observe a significant correlation between working memory (Letter–Number Sequencing Test or computation span) and pattern learning in Session 6 for either patients or control participants (all p values were $>.05$). However, another analysis suggested that control participants with higher Computation Span Test scores showed greater pattern learning than

did those with lower scores. In this analysis, control participants were divided into two groups, high working memory and low working memory, by use of the median total score (10) on the Computation Span Test. These two groups did not differ in terms of age, education, or NART scores (all p values were $>.05$) (see Table 2). A 2 (high vs. low groups) \times 2 (trial type) \times 6 (session) analysis on accuracy data yielded a main effect of trial type, $F(1, 22) = 134.45, p < .01$, and a significant two-way interaction of Group \times Trial Type, $F(1, 22) = 10.91, p < .01$. These results indicated that control participants with higher working memory scores had greater sensitivity to the pattern than did those with lower scores. A similar median-split analysis on data for the patient group did not yield significant results. The median total score on the Computation Span Test for patients was 4.

Is There a Relationship Between Clinical Symptoms and the Acquisition of Sequential Patterns in Schizophrenia?

Correlation analyses were performed for the PANSS subscale scores and the two measures of the ASRT Test discussed above: performance in Session 1 and pattern learning in Session 6. The three PANSS subscale scores reflect the severity of positive symptoms (e.g., hallucinations, delusions), negative symptoms (e.g., blunted affect, social withdrawal), and general psychopathology (e.g., depression, anxiety). The correlations were based on 24 patients. In Session 1, positive symptoms were correlated to response time— $r = .43, p < .05$, for random trials, and $r = .41, p < .05$, for pattern trials—and negative symptoms were correlated to accuracy— $r = -.46, p < .05$, for random trials, and $r = -.46, p < .05$, for pattern trials. Thus, patients with more severe positive and negative symptoms had poorer performance in Session 1. Because patients who are more symptomatic may also have working memory deficits, we reexamined the relationship between symptoms and initial performance using a partial correlation analysis. This analysis showed that positive symptoms were not correlated to speed of responses in Session 1 when working memory was taken into account. In contrast, the relationship between negative symptoms and accuracy remained significant after the effects of working memory were accounted for. Further exploratory tests of the individual items in the negative

Table 2
Characteristics of Control Participants in High and Low Working Memory Groups

Characteristic	High	Low
Sample size	12	12
Age (years)	38.83 (7.59)	42.00 (8.20)
Education (years)	13.33 (1.92)	13.17 (1.59)
National Adult Reading Test score	103.95 (9.03)	102.17 (5.78)
Total span	34.42 (22.25)	5.58 (1.78)

Note. Data are reported as means (SDs) unless otherwise indicated.

subscale revealed that the item of passive or apathetic social withdrawal was correlated to accuracy, $r_s = -.54, p < .01$, for pattern trials, and $r_s = -.52, p < .01$, for random trials. In fact, the severity of patients' passive or apathetic social withdrawal was consistently correlated to accuracy over all six sessions, suggesting a more pervasive effect of negative symptoms on patients' ability to perform this test.

To assess the relationship between clinical symptoms and overall learning of the sequential pattern, we correlated the PANSS subscale measures (positive, negative, and general psychopathology) to pattern learning (i.e., pattern trials minus random trials) in Session 6. Pattern learning was significantly correlated only to scores on the general psychopathology subscale, $r = .43, p < .05$, for the response time measure. This finding indicated that patients with more severe symptoms were less sensitive to regularities in the sequence. Additional exploratory analyses were conducted with a more conservative alpha level ($p < .01$) to determine which items in the subscale were correlated to pattern learning. These analyses revealed that pattern learning was significantly correlated only to the item of somatic concern, $r_s = .56, p < .01$.

Is There a Correlation Between Pattern Learning and Abnormal Movements or Dose of Medication?

Abnormal involuntary movements, such as tardive dyskinesia, can occur in schizophrenia patients who have been treated with antipsychotic medications (Baldessarini et al., 1980). The severity of abnormal movements on the AIMS is rated on a scale from 0 (*none*) to 4 (*severe*). Eighteen of the patients had a severity rating of 0 (no abnormal movements), and 6 of the patients had scores above 0. The mean rating of severity on the AIMS for the entire patient group was 0.50 ($SD = 0.93$), suggesting only mild movement disorders for this group. The AIMS scores were significantly correlated to accuracy in Session 1, $r_s = -.52, p < .01$, for pattern trials, and $r_s = -.48, p < .05$, for random trials. These scores were not correlated to response time in Session 1 or any measure of pattern learning in Session 6. We also observed a correlation between dose of antiparkinsonian medication (benztropine) and accuracy in Session 1, $r = -.61, p < .01$, for pattern trials, and $r = -.58, p < .01$, for random trials. However, this correlation was no longer significant when the AIMS scores were taken into account by use of a partial correlation analysis. These results suggested that abnormal movements rather than medication level accounted for the correlation between antiparkinsonian medication and accuracy in Session 1. Antiparkinsonian medication was not correlated to response time in Session 1 or to pattern learning in Session 6. Abnormal movements may have interfered with initial performance on the ASRT Test, as evidenced by higher error rates in Session 1 for patients with higher AIMS scores. However, abnormal movements were unrelated to pattern learning. There was no correlation between any measure of ASRT Test performance and either antipsychotic medication mea-

sured in chlorpromazine equivalents or the duration of illness measured by the number of years since the first onset of symptoms (p values were $> .05$).

Discussion

This study was designed to characterize the acquisition of sequential information in people with schizophrenia by use of a Serial Response Time Test in which pattern trials alternated with random trials. The patients in this study learned about sequential patterns in the ASRT Test, as evidenced by faster and more accurate responses to pattern trials than to random trials over sessions. Despite extensive exposure to structured sequences, however, schizophrenia patients were impaired in learning compared with control participants.

Although the schizophrenia patients showed impaired performance in the ASRT Test, their performance resembled that of the control participants in several ways. First, both groups learned about the statistical structure of elements in the pattern that extended beyond simple event frequencies. The highest level of structure that both patients and control participants learned about was sequential information about three-trial events or triplets. This finding was shown in an analysis in which responses for random triplets that were consistent with the pattern did not differ from responses for pattern triplets. Thus, it does not appear that pattern learning was impaired in schizophrenia, because the control participants learned a more complex sequence structure than the patients did.

A second similarity between the groups was that the patients' performance in the free generation task did not differ from the control participants' performance. For both groups, there was a tendency to generate a few, albeit significant, number of triplets like those that they had previously encountered during training. The kind of knowledge that is reflected by performance in generation tasks has been a matter of ongoing debate and investigation (Destrebecqz & Cleeremans, 2001; Jiménez, Méndez, & Cleeremans, 1996; Perruchet & Amorim, 1992). There is research to suggest that generation tasks are sensitive to declarative knowledge in sequence learning, but more recent findings show that generation tasks also tap implicit sequence knowledge over which people have little conscious control (Destrebecqz & Cleeremans, 2001). Because tests are not "process pure," it is possible that performance in the generation task studied here was influenced by multiple components, such as motor fluency and declarative knowledge.

The question of whether or not participants had declarative knowledge of the pattern in the ASRT Test was examined by use of a postexperimental interview, and here again, patients performed in a manner similar to that of controls. The results of these interviews revealed that participants in both groups were unable to describe the alternating pattern or notice any regularity in the way in which the target was presented in the ASRT Test (e.g., a higher frequency of some triplets than of others). Insofar as participants were unable to verbalize the pattern, these data suggested that the

learning of sequential patterns in the ASRT Test was not accompanied by declarative knowledge. Although investigators have questioned the sensitivity of the verbal report methodology for detecting explicit knowledge (e.g., Jiménez et al., 1996; Shanks & St. John, 1994), we observed the same findings as those reported here when we used a more sensitive recognition test in which participants sorted all possible triplets into categories depending on how frequently they thought that each triplet had occurred (Marvel, Hovaguimian, & Schwartz, 2001). Implicit sequence learning in the ASRT Test was impaired in schizophrenia patients even when the recognition test revealed that participants had no declarative knowledge of the sequence. Other ASRT Test studies also showed that control participants performed at chance on forced-choice recognition and recognition sorting tasks, providing more evidence that implicit sequence learning occurs in the ASRT Test in the absence of declarative knowledge (Japikse, Howard, & Howard, 2001; Negash, Howard, Japikse, & Howard, 2003). Together, these results rule out the possibility that serial response time learning is impaired in schizophrenia because of group differences in declarative strategies for learning sequential information.

The results of this study yielded some preliminary evidence that working memory plays a role in pattern learning in the ASRT Test. We found that for both patients and control participants, performance on the Computation Span Test was correlated to response time for Session 1 of the ASRT Test. Working memory may be needed early in training, when people use conscious and effortful strategies to learn perceptual-motor mapping in a task (e.g., if a target appears in the rightmost position, then use the right middle finger). Another analysis that indicated that working memory was involved in pattern learning was one that used the median score of the Computation Span Test to split the control group into those with high and low working memory abilities. Implicit learning of sequential patterns occurred to a greater extent for control participants in the high working memory group than for those in the low working memory group. These data replicate previous findings that computation span is correlated to implicit learning (J. H. Howard & Howard, 1997) and provide additional support for the idea that working memory contributes to the acquisition of sequential patterns.

A similar median-split analysis on Computation Span Test scores in the patient group did not yield significant results. Patients with longer memory spans did not learn the pattern better than did those with shorter spans. One reason for this finding may be that memory span scores for the patients were clustered in the low range, limiting our ability to examine pattern learning in a group of patients with high working memory function. Another possibility is that patients did not sustain working memory function throughout the six training sessions to the same extent as did control participants. It appears that after patients used intentional strategies to learn the association between the target and the response (as reflected by correlations between working memory and Session 1 performance), they did not rely or

could not rely, given their deficits, on working memory to improve their pattern learning.

Another issue addressed by this research was the relationship between implicit learning and the severity of the patients' psychiatric symptoms. Two findings emerged. First, negative symptoms were significantly associated with accuracy on the ASRT Test over all six sessions, such that patients with more severe symptoms were less accurate. This correlation may reflect the effects of general information processing deficits on performance in the ASRT Test or the effects of more specific deficits related to perceptual-motor integration functions. The second finding was a significant correlation between pattern learning and somatic concern ratings, with patients who were more symptomatic showing less pattern learning. Given the somewhat unexpected nature of this finding, we undertook a closer examination of the individual patients who made up this group. Perusal of the patients' charts and psychiatric interviews revealed that 7 of the 24 patients (29%) scored 5 (out of 7) on the item of somatic concern, suggesting the presence of a somatic delusion. Somatic delusions may occur because schizophrenia patients draw faulty inferences about their bodily functions (e.g., a patient believed his brain had been removed; a patient believed he could hear his heart valves open and close; a patient believed he had wires in his head that were reading his memories). Hemsley (1994) remarked that an abnormal view of the relationship between events is a prominent feature of delusional thinking. The following description of one of his patients illustrates this point (Hemsley, 1994, p. 110): "Recalling his psychotic experiences, [he] noted that the cooccurrence of two events often led immediately to an assumption of a causal relationship between them. It was as if previous noncooccurrences were completely ignored." Hemsley (1994) suggested that delusional thinking in schizophrenia could result from an alteration in the judgment of the covariation of events. It was therefore intriguing to find that patients who were less sensitive to learning structural relationships (or covariations) between events in the ASRT Test also showed some form of delusional thinking.

Understanding the clinical correlates of implicit learning in schizophrenia will clearly require further attention. Lewicki and colleagues (Lewicki & Hill, 1987; Lewicki, Hill, & Czyzewska, 1992) suggested that intuitive knowledge can influence how people form impressions, draw inferences, and react to situations and people. On the basis of these notions, implicit learning may contribute to social and adaptive functioning in patients with schizophrenia. Future research might examine how these patients acquire intuitive knowledge of regularities in social contexts and how this knowledge relates to adaptive functioning in schizophrenia.

What might account for deficits in implicit learning in the ASRT Test in schizophrenia? One possibility is that learning in this test involves motor sequencing systems that are impaired in schizophrenia. Willingham (1998) suggested that learning in the Serial Response Time Test (a task of motor skill learning) involves increasing the efficiency of a motor control process called *sequencing*. Sequencing sup-

ports learning in a task when the same series of movements are made repeatedly. Motor sequencing is considered a crucial element of learning in the Serial Response Time Test because what is learned is a sequence of motor response locations, as evidenced by poor transfer when response locations (but not spatial cues) are changed (Willingham, 1999; Willingham, Wells, Farrell, & Stemwedel, 2000), and because sequence learning is impaired in patients with diseases of the motor system, such as Huntington's disease (Knopman & Nissen, 1991; Willingham & Koroshetz, 1993) and Parkinson's disease (e.g., Ferraro, Balota, & Connor, 1993; Jackson, Jackson, Harrison, Henderson, & Kennard, 1995).

Schizophrenia patients display multiple abnormal movements that could contribute to deficits in pattern learning in the ASRT Test. These abnormalities include incoordination, stereotypies (repetitive movements), and perseveration (Manschreck, 1986), in addition to the spontaneous involuntary movements associated with tardive dyskinesia. These patients are also impaired on tasks of motor sequencing (Schwartz, Rosse, Veazey, & Deutsch, 1996; Sullivan et al., 2001) and on tasks that require the synchronization of movements or switching from one movement to another (Manschreck, Maher, Rucklos, Vereen, & Ader, 1981). However, it is unlikely that deficits in motor functioning were fully responsible for the difficulties in implicit pattern learning observed in these patients. First, our results suggested that abnormal movements played a minor role only in the initial performance of the ASRT Test (i.e., accuracy in Session 1) and were unrelated to the degree of sequence learning. Second, there is evidence that motor skill learning in another classic task of motor sequencing, the rotary pursuit task, is unimpaired in schizophrenia (Kern et al., 1997). These data suggest that learning in the Serial Response Time Test depends on processes different from or in addition to those involved in motor sequencing in the rotary pursuit task. Finally, although there is strong evidence that the Serial Response Time Test depends on motor functioning, others have suggested that implicit learning in the test is not exclusively dependent on motor functioning but involves nonmotor (perceptual) components as well (Goschke, 1998; J. H. Howard, Mutter, & Howard, 1992; Mayr, 1996).

Another factor that could contribute to deficits in pattern learning in schizophrenia is that implicit learning in the Serial Response Time Test makes high demands on attention and working memory. Early studies of the Serial Response Time Test suggested that implicit learning in this test was largely dependent on attention (Nissen & Bullemer, 1987). Although later work showed that only certain types of sequential patterns required attentional capacity (Cohen, Ivry, & Keele, 1990; Curran & Keele, 1993), findings that learning was reduced under dual-task versus single-task conditions suggested that sequence learning was not entirely an automatic process. In addition, sequence learning depends on selective attention in that attributes of stimuli that predict spatial location do not influence learning unless participants attend and respond to these attributes (Jiménez & Méndez, 1999). Other work has indicated that implicit

sequence learning is related to short-term memory capacity and to the rate of presentation of targets in the sequence. Frensch and Miner (1994) observed that participants with longer memory spans showed better sequence learning. These investigators also found that slower rates of presentation of targets decreased learning (e.g., a response-stimulus interval of 1,500 ms nearly eliminated sequence learning). Longer memory spans and shorter presentation rates affect implicit learning because they allow more information to become available (or activated) at any one time, increasing the likelihood that connections between elements in the sequence will be formed. These data are similar to the present findings, in which people with higher computation spans showed better pattern learning in the ASRT Test than did those with lower spans.

Lower speed of processing and poor attention and working memory are well documented in schizophrenia (Braff, 1993; Gold, Carpenter, Randolph, Goldberg, & Weinberger, 1997; Park & Holzman, 1992; Spindler, Sullivan, Menon, Lim, & Pfefferbaum, 1997). The impairment in working memory in the schizophrenia patients did not correlate with pattern learning. However, it is possible that the impairment in working memory was secondary to processing speed problems, which could have influenced pattern learning. Lower processing speed might have reduced the amount of simultaneously available information needed to learn about covariations among the targets in the ASRT Test, thus reducing the degree of pattern learning for these patients. Problems in processing speed and working memory might also have had an effect on motor responses and response selection in the ASRT Test. If prior elements in the pattern are available in memory, then future items in the pattern are more predictable, and people can prepare their motor responses for the next item (i.e., anticipate future responses). If patients cannot keep several elements in mind at once, then their ability to prepare and select responses will be diminished.

An understanding of the deficits in the ASRT Test in schizophrenia will also depend on identification of the neural basis of implicit learning in this test. Evidence from lesion studies in animals and clinical and brain mapping studies in humans has suggested that implicit learning of visuomotor sequences is mediated by multiple structures, such as motor cortical areas (e.g., supplementary motor area), the striatum, thalamic nuclei, and the cerebellum. For instance, impairments in Serial Response Time Tests in patients with Huntington's disease and patients with Parkinson's disease have provided evidence of a striatal contribution to sequence learning (Ferraro et al., 1993; Doyon et al., 1997, 1998; Knopman & Nissen, 1991). Studies of patients with cerebellar lesions (Doyon et al., 1997, 1998; Gómez-Beldarrain, Garcia-Monco, Rubio, & Pascual-Leone, 1998) and lesion studies in animals (Nixon & Passingham, 2000) have indicated that the cerebellum also is involved in learning of motor sequences. Brain imaging studies have confirmed the critical role of these structures and have suggested that the striatum and cerebellum are involved in the gradual learning and automatization of visuomotor skills (e.g., Doyon et al., 2002; Rauch et al., 1995,

1997; see also Jueptner & Weiller, 1998). The prefrontal cortex has also been implicated in the process of learning of visuomotor sequences. Although this brain area has been associated with explicit sequence knowledge (Hazeltine, Grafton, & Ivry, 1997; Honda et al., 1998), recent findings have also suggested a role for the prefrontal cortex in sequence learning when no explicit awareness of the sequence is detected (Gómez-Beldarrain, Grafman, Ruiz de Velasco, Pascual-Leone, & Garcia-Monco, 2002; Willingham, Salidis, & Gabrieli, 2002).

Many of the above studies examined the neural structures involved in learning of sequential information with deterministic sequences, in contrast to the probabilistic sequences used here. Sequences are deterministic when each element in the pattern is completely predictable from previous elements. They contain no random or unpredictable events. Neural circuits involved in learning of sequential knowledge that is based on the statistical features of items (as in the ASRT Test) may vary to some extent from those involved in learning of deterministic sequences. Greater unpredictability in processing and responding to targets could place high demands on visuospatial attention, selection processes, inhibition of responses, and maintenance of contextual events in working memory. Therefore, learning of higher-order sequential dependencies in the ASRT Test may depend to a greater extent on functional circuits that include prefrontal and parietal cortical areas (Berns, Cohen, & Mintun, 1997; Peigneux et al., 2000).

The results of this study and those of others (Green et al., 1997; Kumari et al., 2002) suggest that implicit learning of sequential knowledge is impaired in schizophrenia. In contrast, several recent studies have suggested that implicit learning in an artificial grammar task (Danion et al., 2001) and in a probabilistic classification task (Kéri et al., 2000) is unimpaired. It is possible that implicit learning in these latter tasks depends less on motor sequencing systems and working memory capacity and involves neural structures different from those involved in the Serial Response Time Test. Along these lines, the recent finding that artificial grammar learning is intact in patients with Parkinson's disease and those with cerebellar lesions (P. J. Reber & Squire, 1999; Witt, Nuhman, & Deuschl, 2002) suggests that implicit learning in this task is mediated by a neural system different from that involved in learning of sequential knowledge.

To date, implicit learning has been studied in only a handful of tasks in schizophrenia. Future research will need to clarify the underlying components of different tasks to better understand why schizophrenia patients are impaired in some tasks and not in others. Our research suggested that people with schizophrenia were less sensitive to regularities in the environment, a finding that could distort their experience (Hemsley, 1994). As implicit learning is the process whereby experience influences memories unknowingly, it will be important to study how deficits in this process shape the judgment and behavior of people with schizophrenia.

References

- Abrams, M., & Reber, A. S. (1988). Implicit learning: Robustness in the face of psychiatric disorders. *Journal of Psycholinguistic Research, 17*, 425–439.
- Aleman, A., Hijman, R., de Haan, E. H. F., & Kahn, R. S. (1999). Memory impairment in schizophrenia: A meta-analysis. *American Journal of Psychiatry, 156*, 1358–1366.
- American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.
- Baldessarini, R. J., Cole, J. O., Davis, J. M., Simpson, M. D., Tarsy, D., Gordos, G., & Preskorn, S. H. (1980). Tardive dyskinesia: Summary of a task force report of the American Psychiatric Association. *American Journal of Psychiatry, 137*, 1163–1172.
- Berns, G. S., Cohen, J. D., & Mintun, M. A. (1997, May 23). Brain regions responsive to novelty in the absence of awareness. *Science, 276*, 1272–1275.
- Blair, J. R., & Spreen, O. (1989). Predicting premorbid I.Q.: A revision of the National Adult Reading Test. *Clinical Neuropsychologist, 43*, 129–136.
- Braff, D. L. (1993). Information processing and attention dysfunctions in schizophrenia. *Schizophrenia Bulletin, 19*, 233–259.
- Braver, T. S., Barch, D. M., & Cohen, J. D. (1999). Cognition and control in schizophrenia: A computational model of dopamine and prefrontal function. *Biological Psychiatry, 46*, 312–328.
- Calev, A. (1984). Recall and recognition in chronic nondemented schizophrenics: Use of matched tests. *Journal of Abnormal Psychology, 93*, 172–177.
- Clare, L., McKenna, P. J., Mortimer, A. M., & Baddeley, A. D. (1993). Memory in schizophrenia: What is impaired and what is preserved? *Neuropsychologia, 31*, 1225–1241.
- Cohen, A., Ivry, R. I., & Keele, S. W. (1990). Attention and structure in sequence learning. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 16*, 17–30.
- Curran, T., & Keele, S. W. (1993). Attentional and nonattentional forms of sequence learning. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 19*, 189–202.
- Danion, J. M., Meulemans, T., Kauffmann-Muller, F., & Vermaat, H. (2001). Intact implicit learning in schizophrenia. *American Journal of Psychiatry, 158*, 944–948.
- Destrebecqz, A., & Cleeremans, A. (2001). Can sequence learning be implicit? New evidence with the process dissociation procedure. *Psychonomic Bulletin & Review, 8*, 343–350.
- Doyon, J., Gaudreau, D., Laforce, R., Jr., Castonguay, M., Bédard, P. J., Bédard, F., & Bouchard, J.-P. (1997). Role of striatum, cerebellum, and frontal lobes in the learning of a visuomotor sequence. *Brain & Cognition, 34*, 218–245.
- Doyon, J., Laforce, R., Jr., Bouchard, G., Gaudreau, D., Roy, J., Poirier, M., et al. (1998). Role of the striatum, cerebellum and frontal lobes in the automatization of a repeated visuomotor sequence of movements. *Neuropsychologia, 36*, 625–641.
- Doyon, J., Song, A. W., Karni, A., Lalonde, F., Adams, M. M., & Ungerleider, L. G. (2002). Experience-dependent changes in cerebellar contributions to motor sequence learning. *Proceedings of the National Academy of Sciences, USA, 99*, 1017–1022.
- Elvevag, B., Weinberger, D. R., & Goldberg, T. E. (2001). Short-term memory for serial order in schizophrenia: A detailed examination of error types. *Neuropsychology, 15*, 128–135.
- Feeney, J. J., Howard, J. H., Jr., & Howard, D. V. (2002). Implicit learning of higher-order sequences in middle age. *Psychology and Aging, 17*, 351–355.

- Ferraro, F. R., Balota, D. A., & Connor, L. T. (1993). Implicit memory and the formation of new associations in nondemented Parkinson's disease individuals and individuals with senile dementia of the Alzheimer type: A serial reaction time (SRT) investigation. *Brain & Cognition*, *21*, 163–180.
- First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (1997). *User's guide for the Structured Clinical Interview for DSM-IV Axis I Disorders—Clinician Version (SCID-CV)*. Washington, DC: American Psychiatric Press.
- Frensch, P. A. (1998). One concept, multiple meanings: On how to define the concept of implicit learning. In M. A. Stadler & P. A. Frensch (Eds.), *Handbook of implicit learning* (pp. 47–104). Thousand Oaks, CA: Sage.
- Frensch, P. A., Lin, J., & Buchner, A. (1998). Learning versus behavioral expression of the learned: The effects of a secondary tone-counting task on implicit learning in the serial reaction time task. *Psychological Research*, *61*, 83–98.
- Frensch, P. A., & Miner, C. S. (1994). Effects of presentation rate and individual differences in short-term memory capacity on an indirect measure of serial learning. *Memory & Cognition*, *22*, 95–110.
- Gold, J. M., Carpenter, C., Randolph, C., Goldberg, T. E., & Weinberger, D. R. (1997). Auditory working memory and Wisconsin Card Sorting Test performance in schizophrenia. *Archives of General Psychiatry*, *54*, 159–165.
- Gómez-Beldarrain, M., Garcia-Monco, J. C., Rubio, B., & Pascual-Leone, A. (1998). Effect of focal cerebellar lesions on procedural learning in the serial reaction time task. *Experimental Brain Research*, *120*, 25–30.
- Gómez-Beldarrain, M., Grafman, J., Ruiz de Velasco, I., Pascual-Leone, A., & Garcia-Monco, J. C. (2002). Prefrontal lesions impair the implicit and explicit learning of sequences on visuo-motor tasks. *Experimental Brain Research*, *142*, 529–538.
- Goschke, T. (1998). Implicit learning of perceptual and motor sequences: Evidence for independent learning systems. In M. A. Stadler & P. A. Frensch (Eds.), *Handbook of implicit learning* (pp. 401–444). Thousand Oaks, CA: Sage.
- Gras-Vincendon, A., Danion, J. M., Grangé, D., Bilik, M., Willard-Schroeder, D., Sichel, J. P., & Singer, L. (1994). Explicit memory, repetition priming and cognitive skill learning in schizophrenia. *American Journal of Psychiatry*, *152*, 1737–1742.
- Green, M. F., Kern, R. S., Williams, O., McGurk, S., & Kee, K. (1997). Procedural learning in schizophrenia: Evidence from the serial reaction time task. *Cognitive Neuropsychiatry*, *2*, 123–134.
- Hazeltine, E., Grafton, S. T., & Ivry, R. (1997). Attention and stimulus characteristics determine the locus of motor-sequence encoding. A PET study. *Brain*, *120*, 123–140.
- Heinrichs, W. R., & Zakzanis, K. K. (1998). Neurocognitive deficit in schizophrenia: A quantitative review of the evidence. *Neuropsychology*, *12*, 426–445.
- Hemsley, D. R. (1994). Perceptual and cognitive abnormalities as the bases for schizophrenic symptoms. In A. S. David & J. Cutting (Eds.), *The neuropsychology of schizophrenia* (pp. 97–116). Hove, United Kingdom: Psychology Press.
- Honda, M., Deiber, M., Ibanez, V., Pascual-Leone, A., Zhuang, P., & Hallett, M. (1998). Dynamic cortical involvement in implicit and explicit motor sequence learning. A PET study. *Brain*, *121*, 2159–2173.
- Howard, D. V., & Howard, J. H., Jr. (2001). When it does hurt to try: Adult age differences in the effects of instructions on sequential pattern learning. *Psychonomic Bulletin & Review*, *8*, 798–805.
- Howard, D. V., Howard, J. H., Jr., Japikse, K., DiYanni, C., Thompson, A., & Somberg, R. (in press). *Sequence learning: Effects of level of structure, adult age, and extended practice. Psychology and Aging*.
- Howard, J. H., Jr., & Howard, D. V. (1997). Age differences in implicit learning of higher order dependencies in serial patterns. *Psychology and Aging*, *12*, 634–656.
- Howard, J. H., Jr., Mutter, S. A., & Howard, D. V. (1992). Serial pattern learning by event observation. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *18*, 1029–1039.
- Jackson, G. M., Jackson, S. R., Harrison, J., Henderson, L., & Kennard, C. (1995). Serial reaction time learning and Parkinson's disease: evidence for a procedural learning deficit. *Neuropsychologia*, *33*, 577–593.
- Japikse, K., Howard, D. V., & Howard, J. H., Jr. (2001). Evaluation of a direct nonverbal measure of declarative sequence knowledge [Abstract]. *Journal of Cognitive Neuroscience Supplement*, *12*, 62.
- Jiménez, L., & Méndez, C. (1999). Which attention is needed for implicit sequence learning? *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *25*, 236–259.
- Jiménez, L., Méndez, C., & Cleeremans, A. (1996). Comparing direct and indirect measures of sequence learning. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *22*, 948–969.
- Jueptner, M., & Weiller, C. (1998, August). A review of differences between basal ganglia and cerebellar control of movements as revealed by functional imaging studies. *Brain*, *121*, 1437–1449.
- Kay, S. R., Opler, L. A., & Fiszbein, A. (1992). *Positive and Negative Syndrome Scale (PANSS) manual*. New York: Multi-Health Systems, Inc.
- Kéri, S., Kelemen, O., Szekeres, G., Bagóczy, N., Erdélyi, R., Antal, A., et al. (2000). Schizophrenics know more than they can tell: Probabilistic classification learning in schizophrenia. *Psychological Medicine*, *30*, 149–155.
- Kern, R. S., Green, M. F., & Wallace, C. J. (1997). Declarative and procedural learning in schizophrenia: A test of the integrity of divergent memory systems. *Cognitive Neuropsychiatry*, *2*, 39–50.
- Knopman, D., & Nissen, M. J. (1991). Procedural learning is impaired in Huntington's disease: Evidence from the serial reaction time task. *Neuropsychologia*, *29*, 245–254.
- Kumari, V., Gray, J. A., Honey, G. D., Soni, W., Bullmore, E. T., Williams, S. C. R., et al. (2002). Procedural learning in schizophrenia: A functional magnetic resonance imaging investigation. *Schizophrenia Research*, *57*, 97–107.
- Lewicki, P., & Hill, T. (1987). Unconscious processes as explanations of behavior in cognitive, personality, and social psychology. *Personality and Social Psychology Bulletin*, *13*, 355–362.
- Lewicki, P., Hill, T., & Czyzewska, M. (1992). Nonconscious acquisition of information. *American Psychologist*, *47*, 796–801.
- Manschreck, T. C. (1986). Motor abnormalities in schizophrenia. In H. A. Nasrallah & D. R. Weinberger (Eds.), *Handbook of schizophrenia* (pp. 65–96). New York: Elsevier.
- Manschreck, T. C., Maher, B. A., Rucklos, M. E., Vereen, D. R., & Ader, D. N. (1981). Deficient motor synchrony in schizophrenia. *Journal of Abnormal Psychology*, *90*, 321–328.
- Marvel, C. L., Hovaguimian, A. E., & Schwartz, B. L. (2001). Implicit learning of spatial and non-spatial sequences in schizophrenia. *Centenary Annual Conference Final Programme & Abstracts*, *585*, 147–148.

- Mayr, U. (1996). Spatial attention and implicit sequence learning: Evidence for independent learning of spatial and nonspatial sequences. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 22, 350–364.
- McKenna, P. J., Tamlyn, D., Lund, A., Mortimer, A. M., Hammond, S., & Baddeley, A. D. (1990). Amnesic syndrome in schizophrenia. *Psychological Medicine*, 20, 967–972.
- National Institute of Mental Health. (1976). Abnormal involuntary movement scale. In W. Guy (Ed.), *ECDEU assessment manual*. Rockville, MD: U.S. Department of Health, Education and Welfare.
- Negash, S., Howard, D. V., Japikse, K. C., & Howard, J. H., Jr. (2003). Age-related differences in implicit learning of non-spatial sequential patterns. *Aging, Neuropsychology, and Cognition* 10, 108–121.
- Nissen, M. J., & Bullemer, P. (1987). Attentional requirements of learning: Evidence from performance measures. *Cognitive Psychology*, 19, 1–32.
- Nixon, P. D., & Passingham, R. E. (2000). The cerebellum and cognition: Cerebellar lesions impair sequence learning but not conditional visuomotor learning in monkeys. *Neuropsychologia*, 38, 1054–1072.
- Park, S., & Holzman, P. S. (1992). Schizophrenics show spatial working memory deficits. *Archives of General Psychiatry*, 49, 975–982.
- Peigneux, P., Maquet, P., Meulemans, T., Destrebecqz, A., Laureys, S., Degueldre, C., et al. (2000). Striatum forever, despite sequence learning variability: A random effect analysis of PET data. *Human Brain Mapping*, 10, 179–194.
- Perruchet, P., & Amorim, M.-A. (1992). Conscious knowledge and changes in performance in sequence learning: Evidence against dissociation. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 18, 785–800.
- Rauch, S. L., Savage, C. R., Brown, H. D., Curran, T., Alpert, N. M., Kendrick, A., et al. (1995). A PET investigation of implicit and explicit sequence learning. *Human Brain Mapping*, 3, 271–286.
- Rauch, S. L., Whalen, P. J., Savage, C. R., Curran, T., Kendrick, A., Brown, H. D., et al. (1997). Striatal recruitment during an implicit sequence learning task as measured by functional magnetic resonance imaging. *Human Brain Mapping*, 5, 124–132.
- Raz, N., Gunning-Dixon, F. M., Head, D., Dupuis, J. H., & Acker, J. D. (1998). Neuroanatomical correlates of cognitive aging: Evidence from structural magnetic resonance imaging. *Neuropsychology*, 12, 95–114.
- Reber, A. S. (1989). Implicit learning and tacit knowledge. *Journal of Experimental Psychology: General*, 118, 219–235.
- Reber, P. J., & Squire, L. R. (1999). Intact learning of artificial grammars and intact category learning by patients with Parkinson's disease. *Behavioral Neuroscience*, 113, 235–242.
- Remillard, G., & Clark, J. M. (2001). Implicit learning of first-, second-, and third-order transition probabilities. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 27, 483–498.
- Rizzo, L., Danion, J.-M., Van Der Linden, M., Grangé, D., & Rohmer, J. G. (1996). Impairment of memory for spatial context in schizophrenia. *Neuropsychology*, 10, 376–384.
- Salthouse, T. A., & Babcock, R. L. (1991). Decomposing adult age differences in working memory. *Developmental Psychology*, 27, 763–776.
- Saykin, A. J., Gur, R. C., Gur, R. E., Mozley, D., Mozley, L. H., Resnick, S. M., et al. (1991). Neuropsychological function in schizophrenia: Selective impairment in memory and learning. *Archives of General Psychiatry*, 48, 618–624.
- Schwartz, B. L., Deutsch, L. H., Cohen, C., Warden, D., & Deutsch, S. I. (1991). Memory for temporal order in schizophrenia. *Biological Psychiatry*, 29, 329–339.
- Schwartz, B. L., Rosse, R. B., & Deutsch, S. I. (1993). Limits of the processing view in accounting for dissociations between memory measures in a clinical population. *Memory & Cognition*, 21, 63–72.
- Schwartz, B. L., Rosse, R. B., Veazey, K., & Deutsch, S. I. (1996). Impaired motor skill learning in schizophrenia: Implications for corticostriatal dysfunction. *Biological Psychiatry*, 39, 241–248.
- Shanks, D. R., & St. John, M. F. (1994). Characteristics of dissociable human learning systems. *Behavioral and Brain Sciences*, 17, 367–395.
- Spindler, K. A., Sullivan, E. V., Menon, V., Lim, K. O., & Pfefferbaum, A. (1997). Deficits in multiple systems of working memory in schizophrenia. *Schizophrenia Research*, 27, 1–10.
- Sullivan, E. V., Fama, R., Shear, P. K., Cahn-Weiner, D. A., Stein, M., Zipursky, R. B., & Pfefferbaum, A. (2001). Motor sequencing deficits in schizophrenia: A comparison with Parkinson's disease. *Neuropsychology*, 15, 342–350.
- Sullivan, E. V., Shear, P. K., Zipursky, R. B., Sagar, H. J., & Pfefferbaum, A. (1997). Patterns of content, contextual, and working memory impairments in schizophrenia and nonamnesic alcoholism. *Neuropsychology*, 11, 195–206.
- Wechsler, D. (1997). *Wechsler Adult Intelligence Scale—Third edition*. San Antonio, TX: Psychological Corporation.
- Willingham, D. B. (1998). A neuropsychological theory of motor skill learning. *Psychological Review*, 105, 558–584.
- Willingham, D. B. (1999). Implicit motor sequence learning is not purely perceptual. *Memory & Cognition*, 27, 561–572.
- Willingham, D. B., & Koroshetz, W. J. (1993). Evidence for dissociable motor skills in Huntington's disease patients. *Psychobiology*, 21, 173–182.
- Willingham, D. B., Nissen, M. J., & Bullemer, P. (1989). On the development of procedural knowledge. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 15, 1047–1060.
- Willingham, D. B., Salidis, J., & Gabrieli, J. D. E. (2002). Direct comparison of neural systems mediating conscious and unconscious skill learning. *Journal of Neurophysiology*, 88, 1451–1460.
- Willingham, D. B., Wells, L. A., Farrell, J. M., & Stemwedel, M. E. (2000). Implicit motor sequence learning is represented in response locations. *Memory & Cognition*, 28, 366–375.
- Witt, K., Nuhsman, A., & Deuschl, G. (2002). Intact artificial grammar learning in patients with cerebellar degeneration and advanced Parkinson's disease. *Neuropsychologia*, 40, 1534–1540.

Received June 19, 2002

Revision received November 26, 2002

Accepted November 27, 2002 ■