Declarative and Procedural Learning in Schizophrenia: A Test of the Integrity of Divergent Memory Systems

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A comparison of learning rates between schizophrenia patients and normals on measures tapping different memory systems may provide clues about relatively preserved areas of learning in schizophrenia. The present study assessed declarative (nonsense syllable list learning) and procedural (ipsum rotar tracking) learning in a group of chronic schizophrenia inpatients and a group of normal adults. Approximately equivalent baselines were obtained for the two groups on both measures. The results revealed a significant group × trial interaction on the declarative memory measure, exemplified by a shallower learning slope for the patient group. For the procedural learning measure, there was no significant group × block interaction; that is, both groups showed similar learning slopes. These findings suggest a relative preservation of selected procedural aspects of learning in schizophrenia.

INTRODUCTION

Some schizophrenia patients, despite the severity of their psychopathology, show a surprising ability to perform a variety of complex visuomotor skills (e.g. artistic drawing). How is it that they can acquire these skills, but not others? Despite the growing awareness of multiple memory systems in the neurology and neuropsychology literatures, the relevance of multiple memory systems to psychopathology has only recently begun to be explored.

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It is widely held that memory can be divided into at least two distinct systems: declarative and procedural memory (Kinsbourne, 1987; Mishkin, Malamut, & Bachavaller, 1984; Roediger, 1990; Schachter, 1987; Squire, 1992; Tulving, 1987; Willingham, Nissen, & Bullemer, 1989). Declarative memory, also called episodic or event memory, involves the conscious recollection of events or episodes from the past, and is typically measured using tests of recall or recognition. Neuro-anatomically, this type of memory appears to be dependent on the integrity of the mesial temporal lobes, hippocampus, anterior and dorsal medial nuclei of the thalamus, mammillary bodies, and the frontal lobes (Milner, Petrides, & Smith, 1983; Mishkin & Appenzeller, 1987).

Procedural memory does not require the conscious recollection of past events. In fact, for this type of learning, one need not even be aware that learning is taking place. Some investigators have described this procedural memory as "automatic", in that it may occur in the absence of directed attention (Tulving, 1987). One type of procedural memory, motor learning, occurs through repeated practice of motor tasks. This type of learning has been measured using such tasks as pursuit rotor tracking or mirror drawing (Butters, Wolfe, Martone, Granholm, & Cermak, 1985). Findings from a recent positron emission tomography (PET) imaging study of right-handed normal adults suggest that procedural (motor) learning of the type involved in pursuit rotor tracking is associated with activation of the left hemisphere including the primary motor, supplementary motor, and pulvinar thalamus areas (Grafton et al., 1992).

Over the past three decades investigations of memory functioning in schizophrenia have focused largely on the assessment of declarative memory. A large number of studies have documented verbal recall deficits in schizophrenia patients by examining their performance on list learning measures (Calev, Korin, Kugelmass, & Lerer, 1987; Culver, Kunen, & Zinkgraf, 1986; Gold, Randolph, Carpenter, Goldberg, & Weinberger, 1992; Koh & Kayton, 1974). Learning on such tasks is typically measured by examining the number of items recalled over a series of learning trials. Although both schizophrenia patients and normals show a learning curve, schizophrenia patients typically show a shallower slope than normals (Goldberg, Weinberger, Pilskin, Berman, & Podd, 1989; Paulsen et al., 1995; Santler & Nordmark, 1971).

Several investigations have assessed procedural memory using the pursuit rotor tracking task in schizophrenia samples, but the results have been mixed. The balance of early investigations, and one recent investigation, reported significant differences between schizophrenia patients and normal controls on pursuit rotor tracking (Eysenck & Frith, 1977; Green, Kern, Williams, Christenson, & Handrich, 1994; Huston & Shakov, 1949). However, several more recent studies have reported similar rates of acquisition between schizophrenia patients and controls on this particular measure (Clare, McKenna, Mortimer, & Baddley, 1993; Goldberg et al., 1993; Granholm, Bartozkoski, Asarnow, & Marder, 1993). For example, Clare et al. (1993) found that a small
group of memory-impaired schizophrenia patients (n = 12) showed rates of acquisition on the pursuit rotor that were comparable to a group of normal controls (matched for age, sex, and IQ estimate). Similarly, Granholm et al. (1993) reported comparable acquisition rates on the pursuit rotor for a group of schizophrenia outpatients (n = 11) and normal controls. Goldberg et al. (1993) found no differences in performance between groups comprising schizophrenia-affected monozygotic twins, their unaffected twin pair (n = 24 pairs), and a group of normal monozygotic twins. The results of these studies suggest a certain degree of integrity in the procedural memory of schizophrenia patients. In contrast, Green et al. (1994) found significant differences in a comparison of the learning slopes of a group of chronic schizophrenia inpatients (n = 20) and a group of normal adults.

Learning rate is a measurement used for the assessment of both declarative and procedural memory. The interpretation of learning rate can be problematic when samples differ substantially in performance at baseline (Granholm et al., 1993) because such differences exacerbate scale attenuation (i.e. floor or ceiling effects). Learning rate can be interpreted more directly when comparison groups are equivalent at baseline. One approach used to achieve baseline equivalence is to employ titration procedures in which test parameters are adjusted so that all subjects are performing at a certain percent of maximum. Such procedures have been employed for measures of procedural memory (pursuit rotor tracking; Hendel, Salmon, Shults, Walicke, & Butters, 1989), but to our knowledge not declarative memory (e.g. list learning). The present study had two primary aims: (1) to approximately equate baseline levels of performance for a group of schizophrenia inpatients and normal adults on measures of procedural (pursuit rotor tracking) and declarative (nonsense syllable list learning) memory; and (2) to compare the learning rates of the two groups on these measures.

METHOD

Subjects

The present study included 18 right-handed adult male inpatients from Camarillo State Hospital and 15 right-handed adult male nursing staff from the same hospital. All patients met criteria for schizophrenia disorder according to DSMIII-R criteria (APA, 1987) based on the Structured Clinical Interview for DSMIII-R (Spitzer, Williams, Miriam, & First, 1990) and portions of the Present State Examination (PSE; Wing, Cooper, & Sarouss, 1974). Interviewers were trained to at least an 85% agreement for symptom presence with the Diagnosis and Psychopathology Unit of the Mental Health Clinical Research Center for the Study of Schizophrenia at UCLA. Handedness was determined by the individual's writing hand. Exclusionary criteria for both groups included: (1) corrected visual acuity of less than 20/30; (2) history of alcohol/substance dependence; (3) previous identifiable neurological disorder; (4) mental
retardation; (5) native language other than English; and (6) age over 55 years. All patients were maintained on neuroleptic medication, and 11 of the 18 patients were also receiving antiparkinsonism medication at the time of testing. Table 1 presents the means for the two groups on selected demographic characteristics, current neuroleptic dose, and selected indicators of chronicity. The patient group included 9 Caucasians, 4 Latinos, 2 Asians, 2 African-Americans, and 1 Native American. The normal adult group included 6 Caucasians, 6 Latinos, 2 African-Americans, and 1 Native American. Male nursing staff were selected to approximate the patients in age and education.

Procedure

Subjects were administered two tasks, a pursuit rotor tracking task and a nonsense syllable (consant-vowel-consonant, CVC) list learning task. The former was used to assess procedural memory, and the latter was used to assess declarative memory.

Pursuit Rotor Tracking Task. The pursuit rotor tracking task requires the subject to maintain contact between the tip of a light-sensitive wand and a lit target area that moves in a circular path, and was administered on a Lafayette Instruments Company Photoelectric Rotary Pursuit Apparatus (Model no. 30014). Time-on-target was measured in milliseconds using a clock counter (Model no. 54003) connected to the rotary pursuit apparatus. Measurement began when the subject made initial contact with the target stimulus. Both the schizophrenic group and the normal group received identical administration procedures. A 20-minute practice trials, which consisted of a series of 20-second practice trials, preceded the test trials. During the practice trials, the speed of the target stimulus was initially set at 10kpm and was increased by 10kpm per trial until two consecutive trials bounded 25% time-on-target (i.e. 5sec). The rpm setting

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Demographic Characteristics for Schizophrenia and Normal Control Groups</th>
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<tr>
<td></td>
<td>Schizophrenia Group</td>
</tr>
<tr>
<td></td>
<td>(SD)</td>
</tr>
<tr>
<td>Age</td>
<td>36.7 (9.0)</td>
</tr>
<tr>
<td>Education</td>
<td>11.6 (3.2)</td>
</tr>
<tr>
<td>Illness duration (yrs.)</td>
<td>17.3 (6.4)</td>
</tr>
<tr>
<td>Length of present hospitalization (mon.)</td>
<td>51.7 (61.5)</td>
</tr>
<tr>
<td>Current neuroleptic dose (chlorpromazine equivalents, mg/day)</td>
<td>1327.6 (689.1)</td>
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that yielded the performance level closest to 25% time-on-target was used for the experimental trials (Heindel et al., 1989).

The experimental trials were administered in six blocks, and each block consisted of four 20-second trials. Subjects received a 10-15 minute rest break between Blocks 2 and 3 and again between Blocks 4 and 5; all other interblock rest intervals were 60 seconds. The dependent measure was time-on-target.

Nonsense Syllable (CVC) List Learning Task - A series of 12 CVCs printed in black ink on 4 x 6 inch (10 x 15 cm) laminated nonlined index cards was developed. Nonsense syllables were used, as opposed to simple concrete nouns, to limit the verbal associative value of the items. The CVCs selected for inclusion in the list had moderate associative strength (ratings ranged from 2.3 to 2.7) (Noble, 1961).

A single session titration and testing procedure similar to that used for the pursuit rotor tracking task could not be employed for nonsense syllable list learning because of potential confounds of proactive interference and fatigue. Hence, a two-stage procedure was developed to equate the groups by roughly matching the two groups' percent CVC recall on trial 1. Initially, we piloted administration procedures by presenting the entire set of 12 CVCs to an independent sample of normal adults and a partially overlapping sample of patients (14 of the 18 included in the study). The results indicated that a presentation of 12 CVCs for the normal controls and 8 CVCs for the schizophrenia patients yielded approximately equivalent percent recall scores for the two groups on trial 1. The patients used for piloting were retested at least six months later to minimize practice effects.

The administration procedures for the CVC list learning task were as follows: All subjects were tested individually by an examiner trained by the senior author. Prior to the first trial presentation, both groups were instructed to remember as many of the nonsense syllables as possible. The normal group received all 12 CVCs, and the schizophrenia group received only the first 8 CVCs. Aside from the number of CVCs presented, both groups received identical administration instructions and procedures. Each CVC was presented individually. For each CVC, the examiner pronounced, spelled, then repronounced the nonsense syllable, instructing the subject to immediately repeat aloud the examiner’s pronunciation and spelling. Following this step, each subject was instructed to print the three letters comprising the nonsense syllable on a prepared answer sheet. This procedure was employed to increase registration of the CVCs and to partially overcome momentary lapses that may draw attention away from the CVCs. The respective sets of CVCs (12 for normal adults; 8 for the schizophrenia patients) were presented over five learning trials. Following each learning trial, subjects in both groups were provided a blank answer sheet and requested to print all those CVCs they remembered. The answer sheet was vertically numbered 1-12 for the normal group, 1-8 for the
schizophrenia group, and had three blank spaces beside each number to correspond to the three letters of the CVC. All subjects were instructed that they need not write the CVCs in the same order as presented. The dependent measure was percent recall for each learning trial.

RESULTS

Pursuit Rotor

For the pursuit rotor tracking task, we initially compared the rpm settings that were derived from the titration procedures for the schizophrenia and normal adult groups [mean of normal group = 62.7 rpm (SD = 16.5); mean of schizophrenia group = 37.2 rpm (SD = 11.9)]. The normal group performed the pursuit rotor tracking task under much faster target speed conditions than the patients (P < 0.001).

The results from the experimental trials of the pursuit rotor tracking task were then analysed using a 2 (groups) × 6 (blocks) repeated-measures ANOVA, and are illustrated in Fig. 1. This analysis failed to yield a significant effect of group, and there was no significant group × block interaction. The lack of an interaction between groups was further supported by examination of the

FIG. 1. Mean time-on-target for schizophrenia patients and normal adults on the pursuit rotor tracking task.
univariate analyses for each block which showed that the two groups did not significantly differ from one another on any of the six blocks of trials. There was, however, a significant effect of block \( F(5,115) = 30.49, \ P < .0001 \) indicating that both groups improved their performance over the six blocks of trials.

We also analysed the data to see whether neuroleptic dose might be related to pursuit rotor learning in the schizophrenia group. There was no relationship between medication dose, measured in chlorpromazine equivalents, and performance change (Block 6-Block 1) in the group of schizophrenia patients. In addition, we compared the performance change (Block 6-Block 1) of those patients who were receiving antiparkinsonian medication versus those who were not. Patients who were not receiving antiparkinsonian medication \( (n = 7) \) showed a trend for more improvement \( (P < .16) \) than those receiving antiparkinsonian medication \( (n = 11) \).

**Nonsense Syllables (CVcs)**

The results of the nonsense syllable list learning exercise were analyzed using a 2 (groups) \( \times 5 \) (trials) repeated-measures ANOVA, and are illustrated in Fig. 2.

![Graph showing percent recall for schizophrenia patients and normal controls on the nonsense syllable list learning task.](image)

**FIG. 2.** Mean percent recall for schizophrenia patients and normal adults on the nonsense syllable list learning task.
The main effect of group was nonsignificant, but the effect of trial [F(4, 124) = 45.32; \( P < 0.001 \)] and the group x trial interaction [F(4,124) = 6.68; \( P < 0.001 \)] were significant. When each trial was inspected individually, no group differences were noted on trials 1, 2, or 3, however significant differences between groups were noted on trials 4 and 5 with the normal controls performing superior to the schizophrenia group (both \( P \) values < 0.05). Thus, these results indicate a shallower learning curve for the schizophrenia group compared to the normal group.

We then examined the correlation between neuroleptic medication dose and CVC list learning (trial 5-trial 1) in the schizophrenia group. Similar to the results found for pursuit rotor tracking, we found no significant relationship between medication dose and CVC list learning. In addition, there was no significant difference on list learning ability between patients who were receiving antiparkinsonian medication versus those who were not.

**DISCUSSION**

In the present study, significant group differences were found between schizophrenia inpatients and normal controls (approximately equated on age and education) on a measure of declarative learning, but not on a measure of procedural learning. On both the declarative and procedural learning measures, the two groups were roughly equated for baseline levels of performance to maximize the ability to compare learning rates.

The finding that our schizophrenia inpatient group showed a shallower learning slope compared to normal adults on a list learning measure is consistent with a large literature (e.g. Calev et al., 1987; Gold et al., 1992; Koh & Kayton, 1974; Paulsen et al., 1996; Saykin et al., 1991; Tamllyn et al., 1992). However, the present study differs from previous ones in that procedures were employed to approximately equate baseline performance (i.e. 35% item recall at trial 1) for both groups. These procedures were introduced to limit scaling influences (i.e. floor and ceiling effects) that could possibly confound the interpretation of results. In addition, administration procedures included several mechanisms (e.g. having subjects say CVCs aloud, print the CVCs on an answer sheet) to maximize initial registration of the material. Despite roughly equivalent baselines (normals = 33.9% recall on trial 1; schizophrenia patients = 37.5% recall on trial 1), our results indicated an inferior learning slope for the schizophrenia group.

Although the two groups were roughly equated in terms of proportion correct, they differed with respect to their initial raw score. It is possible that our finding of a shallower learning slope for the schizophrenia group relative to the control group could be due to gross differences in overall cognitive ability instead of a pattern of deficits that is specific to schizophrenia. Future studies can test this
possibility by selecting a subgroup of normal controls with relatively low performance to enable the groups to be matched on initial absolute performance. Performance deficits on list learning tasks has been associated with the neuropathological involvement of temporal lobe and diencephalic structures (Squire, 1992), and the histopathological documentation of abnormalities in these structures has also been revealed in schizophrenia (Bogetti et al., 1990; Jeste & Loehr, 1989; Kovelman & Scheibel, 1984). More recent findings implicate the importance of frontal systems involvement in the memory impairment of schizophrenia patients. Memory deficits in schizophrenia may involve these structures, or perhaps a disconnection from these structures, as well.

In contrast to our findings on declarative learning, we failed to find significant differences in performance between our group of schizophrenia patients and normal controls on a measure of procedural learning (pursuit rotor tracking). The findings from the present study are consistent with a series of recent studies that also failed to find differences in performance between schizophrenia patients and normal controls on pursuit rotor tracking. A recent study with different patients from our lab (Green et al., 1994) found significant differences between schizophrenia patients and normal controls. One possible reason for the discrepancy could be that, unlike the present study, the study by Green et al. compared patients to college students.

What brain structures might be involved in pursuit rotor tracking? Pursuit rotor tracking is primarily one of perceptuomotor integration involving motor adjustments to visual feedback. Recent evidence from a PET study of cerebral blood flow identified activation of a wide spectrum of neuro-anatomical sites involving primary motor, supplementary motor, premotor, parietal, and cerebellar areas in the execution of pursuit rotor tracking (Grafton et al., 1992). Interestingly, only the left primary motor cortex, the left supplementary motor area, and the left pulvinar thalamus were implicated in learning (all subjects were right-handed). The involvement of cortical regions (premotor cortex) in conjunction with subcortical structures has previously been implicated in motor skill learning (Saint-Cyr & Taylor, 1992), as well as the involvement of other subcortical structures, especially the cerebellum. Cerebellar abnormalities have been shown to affect perceptuomotor performance as required on a slow tracking task similar to the pursuit rotor exercise (Beppu, Nagaoa, & Tanaka, 1987; Beppu, Suda, & Tanaka, 1984). However, it is not clear whether the cerebellum has a significant role in motor learning on the pursuit rotor, or if it is mainly involved with the execution of integrative motor movements.

In summary, the current study is in agreement with a large literature showing significant differences between schizophrenia patients and normal controls in declarative learning. However, our findings failed to find any significant differences between groups on a measure of procedural learning, a finding supported by a series of recent independent studies. Even though the present
study had a small sample size, we see no tendencies in the data to indicate that a larger sample would have yielded different conclusions. The findings from the present study add to an emerging literature supporting the relative integrity of procedural learning in schizophrenia. It is important to note that procedural learning is a rather broad construct that may involve a number of neural circuits, depending on the method of measurement. Hence, even though schizophrenia patients show comparable levels of learning to normal controls on the pursuit rotor, procedural learning deficits may be found with other forms of assessment. Recent data from our lab using another measure of procedural learning, serial reaction time, support this notion.

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