

Procedural Learning in Schizophrenia: Reconciling the Discrepant Findings

Jesús J. Gomar, Edith Pomarol-Clotet, Salvador Sarró, Raymond Salvador, Catherine E. Myers, and Peter J. McKenna

Background: Studies of procedural learning in schizophrenia have been inconsistent, sometimes finding it to be preserved and sometimes impaired. This study examined three factors that could account for the variability among findings: type of task, presence of general intellectual impairment, and the extrapyramidal side effects of neuroleptic treatment.

Methods: Forty-three patients with schizophrenia and 22 normal control subjects were examined with three different paradigms: the pursuit rotor, mirror reading, and probabilistic learning ("weather prediction"). A subgroup of intellectually preserved patients was also examined. Patients with and without tardive dyskinesia and with and without Parkinsonism were also compared.

Results: The schizophrenic patients showed learning comparable to the control subjects on the pursuit rotor and mirror reading but were impaired on the probabilistic learning task. However, this last difference disappeared when the subgroup of intellectually preserved patients was compared with a subgroup of matched control subjects. Patients with and without tardive dyskinesia or Parkinsonism showed similar learning on all three tasks, but patients with tardive dyskinesia showed poorer overall performance than those without.

Conclusions: Procedural learning tends to be preserved in schizophrenia, and when impairment is found, differences in the overall level of intellectual function might be the determining factor.

Key Words: Cognition, extrapyramidal side effects, procedural learning, schizophrenia, tardive dyskinesia

Procedural learning (PL) refers to the acquisition of motor, perceptual, and certain cognitive skills that takes place outside conscious awareness. This form of learning seems to depend, at least to some extent, on basal ganglia function. Thus, functional imaging studies have demonstrated that normal subjects show activation in the basal ganglia during performance of PL tasks (1–3; also 4). Also, patients with disorders such as Huntington's disease (5,6), Parkinson's disease (6–8), and frontostriatal lesions (9) have been found to show impaired PL in a number of paradigms.

A further disorder in which basal ganglia dysfunction is implicated is schizophrenia. This view is based principally on the strong indirect (10) and, more recently, direct (11,12) evidence for a functional excess of dopamine in the disorder. Additionally, some schizophrenic patients show clinical evidence of basal ganglia dysfunction, exhibiting tardive dyskinesia-like involuntary movements (13–15) and Parkinsonism (16) even when they have never been exposed to neuroleptic drug treatment. For these and other (e.g., theoretical) reasons, schizophrenia is often characterized as a frontostriatal disorder (17,18).

On these grounds, it might be expected that PL would be impaired in schizophrenia. However, until recently, PL seemed to form an exception to the rule that schizophrenic patients are impaired on virtually all cognitive tasks (19). Thus, most studies using the proto-

typical PL task, the pursuit rotor, have found that patients improve their performance at the same rate as normal control subjects (20–23). Procedural learning has also been found to be preserved in a perceptual-motor task, prism adaptation (24), and nonmotor paradigms such as mirror reading (23,25) and learning a rule-based artificial grammar (26,27). Nevertheless, some studies have documented impaired PL in schizophrenia. Two studies found evidence that schizophrenic patients learn more slowly than control subjects on the probabilistic classification or "weather prediction" task, where subjects have to learn whether it will "rain" or "shine" on the basis of stimuli (geometric forms) that are predictive of the two conditions, but only probabilistically (26,28) (although the impairment was somewhat equivocal in the latter study). Impairment has also been found on the serial reaction time task, where subjects gradually learn a sequence of key presses without conscious awareness (29–31). Reduced PL has not been a uniform finding on these two tasks, however, and some studies have reported normal rates of learning (28,32–35).

What accounts for these discrepancies is unclear. Foerde *et al.* (28) have proposed, on the basis of evidence that different corticostriatal loops subserve motor and cognitive functions (36,37), that the nature of the PL task is the important factor: they found that schizophrenic patients were impaired on a cognitive PL task, weather prediction, but not on a motor one, the serial reaction time task. Another potentially relevant factor is general intellectual impairment, which is present to some extent in many schizophrenic patients (38–40), and would normally be expected to depress performance on any and all specific neuropsychological tasks. A third possible explanation relates to neuroleptic drug treatment, which has important side effects on basal ganglia function, including tardive dyskinesia and Parkinsonism. Granholm *et al.* (21) found that schizophrenic patients with tardive dyskinesia showed less learning on the pursuit rotor than those without, although this finding was not replicated in another study (41). Other studies have found that patients taking atypical or second-generation antipsychotic drugs—which do not cause Parkinsonism or cause it to a lesser extent than typical

From the Benito Menni Complex Asistencial en Salut Mental (JJG, EP-C, SS, RS, PJM); Neuroscience Program (JJG), Universitat Autònoma de Barcelona, Barcelona; Centro de Investigación Biomédica en Red de Salud Mental (JJG, EP-C, SS, RS, PJM), CIBERSAM, Madrid, Spain; and the Department of Psychology (CEM), Rutgers University-Newark, Newark, New Jersey.

Address correspondence to: Jesús J Gomar, M.S., Benito Menni CASM, Antoni Pujadas 38, 08830 Sant Boi de Llobregat, Barcelona, Spain; E-mail: jgomar@hospitalbenitomenni.org.

Received Oct 24, 2009; revised Jul 5, 2010; accepted Jul 15, 2010.

or first generation drugs—show better PL in both motor (42–44) and nonmotor tasks (45).

The aim of the present study was to determine whether and to what extent these three factors might account for the variability in the PL findings in schizophrenia. We used a range of different tasks and also examined the degree to which general intellectual impairment and presence of extrapyramidal side effects contributed to any impairment found.

Methods and Materials

Participants

The patient sample consisted of 43 nonelderly patients who met DSM-IV criteria for schizophrenia, on the basis of interview by two psychiatrists plus review of case notes. Exclusion criteria were current IQ < 80, presence of neurological disorder, history of head injury, and substance dependence within the past 5 years. All were taking antipsychotic medication (6 typical antipsychotics, 19 atypical antipsychotics, 18 both types). The following antipsychotics were considered atypical: clozapine, olanzapine, risperidone, amisulpride, quetiapine, and aripiprazole. All patients were in relatively stable clinical condition at the time of testing.

Twenty-two control participants were recruited from hospital staff and the local community. They met the same exclusion criteria as the patients. They were interviewed to verify that they had no history of major psychiatric disorder and that they were not taking any psychotropic medication. None reported a history of alcohol or drug abuse/dependence.

IQ (premorbid IQ in the patients) was estimated with the Word Accentuation Test (TAP) (46), a test analogous to the English National Adult Reading Test (47); in this, the subject has to pronounce irregular Spanish words whose accents have been removed. Current IQ was measured with four subtests of the Wechsler Adult Intelligence Scale III (vocabulary, similarities, block design, matrix reasoning).

Motor disorder was rated from videotapes of patients who were examined following a standardized procedure. Two raters who were not otherwise involved in the study scored these by consensus with standard scales (48,49).

PL Assessment

Testing was carried out over two sessions lasting 1–1.5 hours, separated by 1 week. The tasks were administered by a single investigator who had no knowledge of the patients' motor ratings.

Motor PL (Pursuit Rotor). We used a computerized version of the task (Life Science Associates, New York, New York). Subjects had to follow a moving target around a rectangular track with a mouse held in their preferred hand. Each trial lasted 20 sec with a 5-sec intertrial interval. Subjects were given six blocks of four trials each, interspersed with 20/30 min of other testing after every two blocks. We equated the initial level of performance between the patients and control subjects, so that both groups reached a criterion of being able to maintain contact with the target approximately 20%–25% of the time. Testing was repeated 1 week later.

Perceptual PL (Mirror Reading). Subjects had to read triads of 8- to 10-letter nouns printed in mirror script. These were selected from the computerized Spanish lexicon (50) according to their very low frequency (2–10) in public reading format. Words in each triad were chosen so that there was no obvious semantic or phonemic relationship between them. Subjects read six blocks of 10 word triads with a 1-min interblock rest period. Five triads were repeated across blocks, and five were unique to each block. To control for word difficulty differences, we randomized the order of presenta-

tion of the blocks for each subject. We also randomized the order of presentation within every repeated triad. Testing was repeated 1 week later.

Probabilistic Classification Learning (Weather Prediction). In this task (51,52) subjects saw combinations of cues (1–3 cards displaying simple geometric shapes in different colors) and had to predict two possible outcomes (rain or sun). Each card was associated with one of the two outcomes with a fixed probability, calculated according to the conditional probabilities of each outcome and card occurring together (for a detailed description of the task see Gluck *et al.* (53). Feedback was provided to signal a correct or incorrect response. The sequence of cue combinations appearing on each trial was randomized for each subject, with the constraints that the same cue combination could not appear twice in succession and that each outcome did not occur more than five times in succession. Because of the probabilistic nature of the task, a cue combination was sometimes followed by the less strongly associated outcome. Therefore, responses were scored as "optimal" (i.e., on the basis of whether the participant predicted the weather outcome most often associated with the current pattern on previous trials), irrespective of whether or not the response correctly predicted the actual weather on any given trial. Data were analyzed at 50 trials, as in previous studies using this task. As advocated by Myers (personal communication) we also continued testing to 200 trials, the minimum number that allows the subject to experience enough trials to be exposed to all the cues with the designated probability that each cue predicts the outcome.

Data Analyses

Primary analyses were by means of repeated measures analyses of variance (ANOVAs). Data were arc-sin transformed for the weather prediction task, because they were in the form of proportions.

To examine the influence of general intellectual impairment on differences between patients and control subjects, we followed the procedure used by Weickert *et al.* (33). Specifically, we examined subgroups of patients and control subjects that were matched to within 5 years of age and education, within five points on Wechsler Adult Intelligence Scale III Full Scale IQ estimate, and within three points on TAP score.

Patients with tardive dyskinesia, according to the criteria of Schooler and Kane (54), were compared with those without. Presence of Parkinsonism was determined with analogous criteria (49).

Results

Demographic findings for the patients and control subjects and the clinical features of the patients are summarized in Table 1. Patients and control subjects were matched for age and years of education. There were trend-level differences in gender ratio [$\chi^2(1) = 2.90; p = .09$]. The patients had a significantly lower TAP score [$t(63) = 2.18; p = .03$] and current IQ [$t(63) = 3.29; p = .002$] than the control subjects.

In the IQ matched subsample there were 22 patients (mean age 44.49 [SD = 5.07]; mean IQ 98.91 [SD = 7.54]; mean TAP score 24.18 [SD = 2.89]) and 22 control subjects (mean age 47.00 [SD = 13.51]; mean IQ 102.82 [SD = 7.66]; mean TAP score 23.36 [SD = 4.13]).

Motor PL (Pursuit Rotor)

One control and seven schizophrenic patients were unable to reach the criterion. One control also had missing data for week 2 and was excluded. The two groups were significantly different in target rotation speed [$t(54) = 3.31, p = .001$]. A 2 (group) $\times$ 6 (trial block) $\times$ 2 (week) repeated measures ANOVA with mean time on

Download English Version:

<https://daneshyari.com/en/article/6228794>

Download Persian Version:

<https://daneshyari.com/article/6228794>

[Daneshyari.com](https://daneshyari.com)