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Impaired automatization of a cognitive skill in first-degree relatives of patients with schizophrenia

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ABSTRACT

We studied healthy, first-degree relatives of patients with schizophrenia to test the hypothesis that deficits in cognitive skill learning are associated with genetic liability to schizophrenia. Using the Weather Prediction Task (WPT), 23 healthy controls and 10 adult first-degree Relatives Of Schizophrenia (ROS) patients were examined to determine the extent to which cognitive skill learning was automated using a dual-task paradigm to detect subtle impairments in skill learning. Automatization of a skill is the ability to execute a task without the demand for executive control and effortful behavior and is a skill in which schizophrenia patients possess a deficit. ROS patients did not differ from healthy controls in accuracy or reaction time on the WPT either during early or late training on the single-task trials. In contrast, the healthy control and ROS groups were differentially affected during the dual-task trials. Our results demonstrate that the ROS group did not automate the task as well as controls and continued to rely on controlled processing even after extensive practice. This suggests that adult ROS patients may engage in compensatory strategies to achieve normal levels of performance and support the hypothesis that impaired cognitive skill learning is associated with genetic risk for schizophrenia.

1. Introduction

Consistent with the hypothesis that the pathophysiology of schizophrenia involves dysfunction of corticostriatal circuits (e.g., Kleist, 1960; Buchsbaum, 1990; Buchanan, 1993), patients with schizophrenia perform poorly on cognitive skill learning tasks that tap corticalstriatal networks. Skill learning involves the improvement of performance with practice on a task and is demonstrated by reduced reaction time or increased accuracy. The corticostriatal system plays an important role in cognitive skill learning (Heindel et al., 1989; Knowlton et al., 1996; Doyon et al., 2009; Peigneux et al., 2000) and involves the caudate nucleus, dorsolateral prefrontal cortex, and ventral striatum/orbitofrontal cortex (Aron et al., 2004; Poldrack et al., 2001, 1999).

Several studies have lent support to the idea that patients with schizophrenia show deficits in cognitive skill learning using tasks such as the Tower of Toronto and the Tower of Hanoi (Gimenez et al., 2003; Schroder et al., 1996; Purdon et al., 2003). Another cognitive skill learning task is the Weather Prediction Task (WPT; Knowlton et al., 1994), a probabilistic classification task that requires participants to learn probabilistic associations between cues and binary outcomes by attending to visual stimuli presented on a computer screen, after which they are provided feedback about the correctness of their response (Fig. 1). Because the Tower of Toronto and the Tower of Hanoi demand considerable executive control resources and can involve learning strategies dependent on declarative cognitive processes through the application of stateable rules or algorithms (Winter et al., 2001), impairments on these tasks in patients with schizophrenia may reflect deficits in these domains. Due to its relatively simple task demands and the fact that there is no algorithm or rule that can potentially provide a solution, the WPT may be a more specific test of cognitive skill learning that is characterized by incremental learning that relies on corticostriatal function.

Performance on the WPT is impaired in patients with schizophrenia (Foerde et al., 2008; Keri et al., 2005; Horan et al., 2008;

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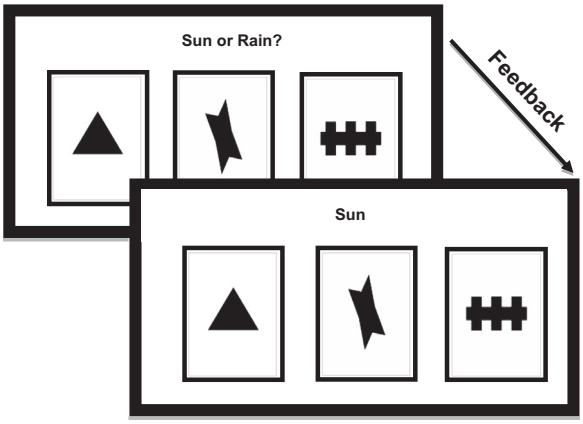

Fig. 1. The WPT. Participants were told to predict the weather (sun or rain) based on cues. On every trial between one and three cues (out of four possibilities) could appear, yielding 14 possible combinations. The cues were probabilistically related to the outcomes. The association of the different cues with different probabilities was randomized across participants. The cue strength of each of the 14 resulting stimuli were such that the overall probability associating each cue with sun or rain was 0.727, 0.556, 0.409, and 0.280 across the task. The cues are shown on the screen for a maximum of 3 s, the feedback is shown on the screen for 1 s, and the time between trials is 0.5 s. During the secondary task, a subject hears a series of high and low pitch tones during the task and has to count the number of high pitch tones while completing the WPT. Between one and three tones are heard during each trial of the secondary task.

Weickert et al., 2002). However, these deficits may be related to the anti-psychotic medications these patients were receiving to control their psychotic symptoms. Anti-psychotic medications have effects on striatal structure (i.e., enlargement of the volume of the basal ganglia) and alter striatal D^2 receptors (Paquet et al., 2004; Kumari et al., 2000). It is possible that these medications impair striatal function, resulting in the impaired cognitive skill learning observed in patients receiving anti-psychotic treatment. In other studies, treatment with antipsychotic medication improves performance on skill learning tasks (Harvey et al., 2000; Serper et al., 1990), and thus may mask deficits. Thus, whether impaired cognitive skill learning reflects liability to schizophrenia remains unclear because of potential medication effects.

Since schizophrenia has a strong genetic basis, findings of impaired cognitive skill learning in patients raise the possibility that genes that contribute to schizophrenia may affect striatal functioning as well. Studying healthy relatives of patients with schizophrenia eliminates the possible confounding effects of medication and can provide valuable insight into the etiology of this disease. Cognitive skill learning in relatives of patients with schizophrenia (ROS) has been less well examined than in patients themselves. Weickert et al. (2010) compared patients with schizophrenia to their healthy adult siblings and to controls on the WPT. While the patients demonstrated a severe learning deficit compared to controls, the siblings of patients generally performed in the normal range. However, the sibling group included more poor performers than the control group. Wagshal et al. (2012) compared adolescent siblings of patients with Childhood Onset Schizophrenia (COS) to adolescent controls and found significant performance differences early and late in training. Early in training siblings revealed a severe learning deficit compared to controls, and even after extensive training the COS siblings reached a lower level of asymptotic performance than controls. COS is a more severe and more familial form of schizophrenia than the adult onset form (Asarnow et al., 2001; Asarnow and Asarnow, 1994; Nicolson and Rapoport, 1999) and this may have contributed to the greater deficit found in Wagshal et al. (2012). Age may have also played a role, in that the participants in Wagshal et al. (2012) were adolescents. It is possible that the impairment in the COS siblings represents a developmental delay and not an enduring delay that is present in adulthood.

In this study we examined the performance of healthy, adult first-degree ROS patients on the WPT. Previous work suggests that there may be only subtle deficits in WPT performance in this group. To detect relatively subtle deficits in ROS patients we assessed the degree to which performance becomes automatic as training progresses. Automatization of a skill is achieved when the skill can be executed without making demands for executive control and effortful processing. A major characteristic of automaticity is when concurrent performance of a secondary task does not interfere with primary task performance of a skill (Posner and Snyder, 1975). Automaticity is important in everyday life and is critical for handling unexpected cognitive challenges, for problem-solving, and for performing concurrent activities that are required in many social and work settings (Green et al., 2000; Harvey et al., 2006). Thus, evidence of reduced automatization of cognitive skills in ROS patients may have implications for daily life activities.

There is agreement in the literature that individuals with schizophrenia or schizotypal personality disorder have diminished processing resources (Asarnow et al., 1995; Braff, 1981, 1985; Harvey et al., 1996, 2006; Holzman, 1987; Moriarty et al., 2003; Nuechterlein, 1991), and that the ability of individuals with schizophrenia to automate skills is more impaired than controls. Insufficient processing resources to handle higher processing loads can result in cognitive impairment in schizophrenia patients (Asarnow et al., 1991; Asarnow and Sherman, 1984; Gjerde, 1983; Sherman and Asarnow, 1985). Patients with schizophrenia may reach the limits of their available resources at lower processing loads and have fewer available resources than healthy controls (Asarnow, 1999). Processing resources are used when an individual is first learning a skill. With practice, learning becomes automated and makes fewer demands on available resources (Schneider et al., 1984; Asarnow, 1999; Granholm et al., 1996). Even if there are no overt impairments in the ROS patients in this study, their performance may be less automatic than that of controls and thus more sensitive to the effect of a concurrent task.

2. Methods

2.1. Participants

Ten adults who were first-degree relatives of patients diagnosed with schizophrenia (ROS) and 23 adult controls that were matched in age and gender to the relatives participated in the experiment (Table 1). Four controls and two relatives were excluded from analyses based on computer malfunction or not responding on more than 10% of the trials. All participants provided informed consent according to the procedures approved by the University of California, Los Angeles (UCLA) Human Subjects Committee and were paid for their participation. Relatives of schizophrenia probands were recruited based on their previous participation in family studies at UCLA. Families of potential control participants were recruited through online advertisements, flyers, and by randomly calling families found through a commercially available list of households within a 25-mile radius of UCLA (Survey Sampling Inc., Fairfield, CT, USA). All participants in both groups were screened and participants were excluded if there was a history of prior treatment of

Table 1
Demographics of the controls and relatives.

Variable	Controls ($n=19$)		Relatives ($n=8$)	
	M	S.D.	*M*	S.D.
Age	40.00	5.61	39.25	6.90
Gender[a]	5	14	2	6
Vocabulary[b]	55.32	8.50	42.20	9.20
Blocks	55.42	10.72	44.50	8.67

[a] Men/women.
[b] WASI vocabulary subtest (missing three relatives).