Available online at www.sciencedirect.com
ScienceDirect
Schizophrenia Research 99 (2008) 200–207
SCHIZOPHRENIA RESEARCH
www.elsevier.com/locate/schres

How to find the way out from four rooms? The learning of "chaining" associations may shed light on the neuropsychology of the deficit syndrome of schizophrenia

Patricia Polgár [a], Márta Farkas [a], Orsolya Nagy [b], Oguz Kelemen [b], János Réthelyi [a], István Bitter [a], Catherine E. Myers [c], Mark A. Gluck [d], Szabolcs Kéri [a,*]

[a] *Semmelweis University, Department of Psychiatry and Psychotherapy, Budapest, H1083, Balassa u. 6., Hungary*
[b] *Bács-Kiskun Country Hospital, Psychiatry Unit, Kecskemét, Hungary*
[c] *Department of Psychology, Rutgers University, Newark, NY, USA*
[d] *Center for Neuroscience, Rutgers University, Newark, NY, USA*

Received 24 April 2007; received in revised form 20 June 2007; accepted 30 June 2007
Available online 10 August 2007

Abstract

Recent meta-analytic evidence suggests that clinical neuropsychological methods are not likely to uncover circumscribed cognitive impairments in the deficit syndrome of schizophrenia. To overcome this issue, we adapted a cognitive neuroscience perspective and used a new "chaining" habit learning task. Participants were requested to navigate a cartoon character through a sequence of 4 rooms by learning to choose the open door from 3 colored doors in each room. The aim of the game was to learn the full sequence of rooms until the character reached the outside. In the training phase, each stimulus leading to reward (open door in each room) was trained via feedback until the complete sequence was learned. In the probe phase, the context of rewarded stimuli was manipulated: in a given room, in addition to the correct door of that room, there also appeared a door which was open in another room. Whereas the training phase is dominantly related to basal ganglia circuits, the context-dependent probe phase requires intact medial-temporal lobe functioning. Results revealed that deficit and non-deficit patients were similarly impaired on the probe phase compared with controls. However, the training phase was only compromised in deficit patients. More severe negative symptoms were associated with more errors on the training phase. Executive functions were unrelated to performance on the "chaining" task. These results indicate that the deficit syndrome is associated with prominently impaired stimulus–response reinforcement learning, which may indicate abnormal functioning of basal ganglia circuits.

Keywords: Schizophrenia; Deficit syndrome; Habit learning; Basal ganglia; Medial-temporal lobe; Reward

1. Introduction

The heterogeneity of patients is one of the most fundamental problems in schizophrenia research. A particularly important milestone in the field was the introduction of the concept of the deficit syndrome. According to Carpenter and Kirkpatrick (1988), schizophrenia patients with deficit syndrome are characterized by enduring negative symptoms, including flattened affect, anhedonia, poverty of speech, curbing of interest, lack of sense of purpose, and decreased social drive. These symptoms are not accounted for by depression, anxiety, medication side effect, positive symptoms or psychosocial deprivation.

* Corresponding author. Tel.: +36 20 448 3530.
E-mail address: szkeri@phys.szote.u-szeged.hu (S. Kéri).

0920-9964/$ - see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.schres.2007.06.027

Although the construct validity of the deficit syndrome has been supported by various clinical, epidemiological, and biological findings (Kirkpatrick et al., 2001), a clear neurocognitive profile of the syndrome is still missing. Originally, Buchanan et al. (1994) proposed that frontal and parietal functions are especially impaired in deficit patients, but data from some subsequent studies failed to support this hypothesis (e.g. Brazo et al., 2002; Galderisi et al., 2002; Seckinger et al., 2004; Tiryaki et al., 2003). In a meta-analysis of 13 studies, Cohen et al. (2006) found that deficit patients were globally more neuropsychologically impaired than non-deficit patients, with the largest differences in olfaction and social cognition. Therefore, more precise cognitive neuroscience methods are warranted to find potentially specific differences between deficit and non-deficit patients.

To achieve this aim, we used a "chaining" association task originally developed by Shohamy et al. (2005) and Nagy et al. (2007a). The task is motivated by evidence suggesting that the medial temporal lobe (MTL) and the basal ganglia (BG) play distinct roles in learning and memory. The MTL, including the hippocampus, is important in declarative memory functions, whereas the BG is essential for learning habits and skills, such as associations between stimuli and responses (Squire et al., 2004; Yin and Knowlton, 2006). The gradual learning of cognitive habits and skills requires the processing of feedback and reinforcement following decisions and responses. Although the MTL may not be necessary for such reinforcement-based stimulus–response learning, it is important in more complex situations when familiar stimuli are presented in a novel context (Manns and Eichenbaum, 2006). For example, one can easily learn that pressing a blue switch leads to the turning on of the air conditioner in the bedroom (trial-by-error stimulus–response learning based on feedback). However, it is possible that in the kitchen (novel context) the blue switch has a different role. In this case, the non-flexible stimulus–response habit may lead to erroneous consequences, and the context must be taken into consideration for a successful behavior.

In patients with Parkinson's disease, Shohamy et al. (2005) and Nagy et al. (2007a) demonstrated that the BG are involved in the learning of sequential ("chaining") stimulus–response associations, in which each link in a sequence of stimuli leading to reward is trained step-by-step using feedback after each partial sequence is executed, until the complete sequence is learned. During the "chaining" task, participants were required to learn a sequence of events leading to reward. In the first phase of this task, the computer screen showed a room (room 1) with 3 doors (A, X, Y), each bearing a colored card; the participant was required to choose one of these doors by guiding a cartoon character (Fig. 1). Choosing the open

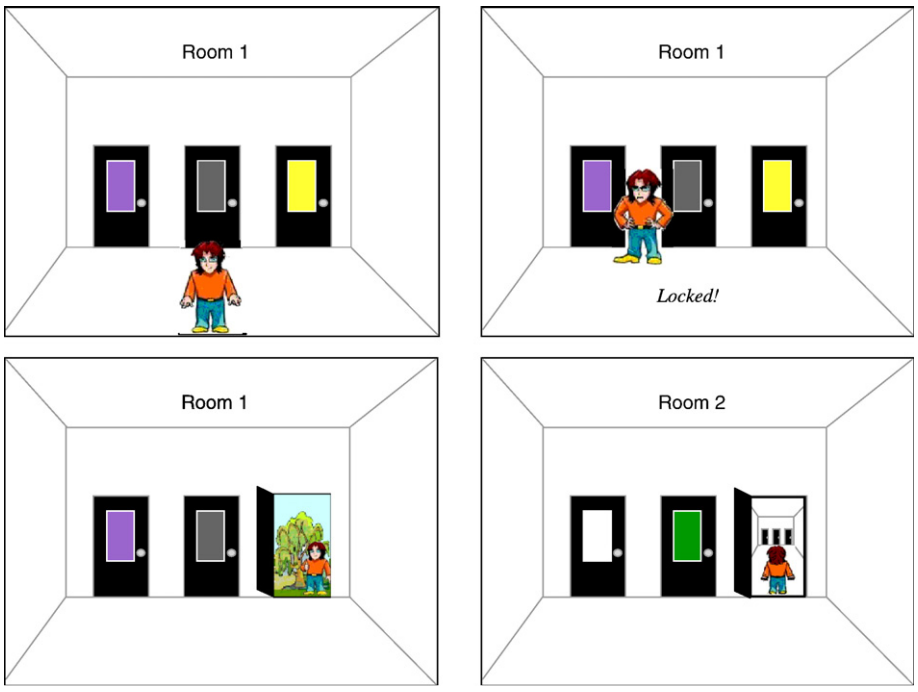

Fig. 1. Display of the "chaining" task. Upper row: The participants chose the closed door in room 1. Lower row, left panel: The participant chose the open door in room 1 and Kilroy reached outside. Lower row, right panel: In room 2, the participant chose the open door and Kilroy entered into room 1.