The Forward Testing Effect in Spatial Route Learning in Patients with Schizophrenia

Ma Xiaofeng¹, Tan Yaoyao¹, Li Tiantian¹, Liu Minghui¹, and Zhang Jing¹

¹Northwest Normal University

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Abstract

It is not known whether patients with schizophrenia can improve their ability to learn new information through tests. We conducted two experiments—to explore the forward testing effects in schizophrenic patients in learning a new route—with 124 schizophrenic patients and a control group of 124 randomly selected healthy. All participants were tasked with learning a two-dimensional planar route map consisting of four lists (Experiment 1) and three-dimensional video spatial route information (Experiment 2). Results from Experiment 1 demonstrated that in a two-dimensional planar route map, both schizophrenic and healthy participants recalled the spatial route information under the test condition versus the repetitive learning condition. In Experiment 2, we used three-dimensional video spatial route information and obtained the same results found in Experiment 1. This study suggests that by using preposed tests, patients with schizophrenia could suppress proactive interference and gain general benefits, including forward-backward effects of retrieval practice. Therefore, tests may be a powerful tool for improving learning and memory in patients with schizophrenia.

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Keywords: schizophrenic patient, forward test effect, spatial memory, route information

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Introduction

Patients with schizophrenia have previously been demonstrated to experience retrieval inhibition in memory recall. Additionally, it is difficult to suppress the appearance of interference information (Soriano, Jiménez, Román, & Bajo, 2009), ignore irrelevant targets, suppress dominant responses, as well as intrusive or unwanted thoughts, distracting memories, or interfering mental images (Weisbrod et al., 2000). Waters et al.(2003)

found evidence of an inhibitory defect in schizophrenic patients when they were asked to suppress current irrelevant memories. This is a specific inhibitory defect in patients with medial orbitofrontal lesions and cognitive impairment (Waters, Badcock, Maybery, & Michie, 2003). Memory rehabilitation therapy emphasizes learning strategies to improve the normal life of patients with cognitive impairments after their recovery (Medalia, et al., 2001; Mark, et al., 2002; Patterson, et al., 2022), including free recall tests, memory judgment, classification and chunking, visualization and selected mnemonic tools, visual and auditory sequential recall, narrative recall, images, and other memory techniques. Experimental studies in cognitive psychology and neuropsychology have also demonstrated the critical role of forward testing in improving learning and memory in healthy individuals and clinical patients (Pastötter, Weber, & Bäuml, 2013).

Forward testing effects indicate that testing in the learning process reduces proactive interference from previously learned materials and promotes the retention of new information in subsequent learning (Aslan, & Bäuml, 2015; Yang, Potts, & Shanks, 2018;Szpunar, McDermott, & Roediger, 2008; Weinstein, McDermott, & Szpunar, 2011). These effects are not limited to healthy individuals. In patients with severe TBI (Traumatic brain injury), previous research demonstrates that retrieving previously learned information helps improve retention rates of subsequent learning of new information with effect sizes comparable to that in the control group (Pastotter, Weber, & Bauml, 2013). To date, it has not been determined whether the forward effects of tests are applicable to clinical patients with cognitive impairments, such as patients with schizophrenia.

Impaired spatial cognitive function may be a more severe form of cognitive dysfunction in schizophrenia (Zhang, Chen, Yang & Liu, 2013). Previous studies have found that schizophrenia patients are generally impaired in spatial working memory tasks (Keefe, Lees Roitman & Dupre, 1997; Spitzer, 1993) and are less accurate in eye movement tests of spatial working memory (McDowell& & Clementz, 1996; Park& & Holzman, 1992). Chev and Tek et al (2002). used the spatial working memory span test and found that schizophrenia patients' scores were significantly lower than those of healthy participants, indicating that patients with schizophrenia had temporary defects in spatial information processing (Tek, et al., 2002; Chev, & Lee, 2002). In the backward masking task designed to assess visual processing channels alone, patients with schizophrenia showed deficits in the spatial location task but not in the letter identification task (Cadenhead; denhead, Serper & Braff, 1998). Similarly, in a study of impaired spatial background memory in patients with schizophrenia (Danion et al., YEAR), results demonstrate that they were more impaired in location memory tasks than in object identification tasks, and to an even greater extent in spatial environment location memory tasks (Danion, Rizzo, Linden, Grange, & Rohmer, 2005). A larger exclusion effect (Bansal et al., 2020) was observed when individuals with schizophrenia were asked to remember spatial locations near consecutive visible landmarks. Therefore, this study intends to investigate whether schizophrenia patients with impaired spatial location memory can improve spatial location memory through preposed tests.

Spatial navigation tests have great potential for clinical diagnosis and intervention (Zhang, Hai, & Li, 2019). Spatial navigation refers to the process of searching for and memorizing routes in familiar or unfamiliar surroundings (Burgess, Maguire, & O'Keefe, 2002). As a high-level cognitive process, spatial navigation relies on several different basic cognitive processes, including vision, proprioception, spatial representation, etc. (Wolbers & Hegarty, 2010). Route learning is a type of spatial navigation that reflects an understanding of a specific route in the environment. It is also the learning of route information on reaching one location from another, usually consisting of a series of landmarks and movements to reach the destination (Siegel & White, 1975). Currently, it is a widely used skill, especially for professionals, such as taxi drivers, bus drivers, and pilots. Moreover, impaired orientation due to dementia or other neuropsychological disorders. such as schizophrenia, also verifies the important role that navigation plays in everyday life. In addition, the learning of route information in daily life is not limited to a single scene; in space, we always move from one scene to another, and route information is thus always cumulative. When we memorize a route's information from multiple directions, the route information of previous directions or scenes interferes with subsequent information. Previous studies have found that for healthy individuals, when learning multiple routes, preposed tests can reduce interference from previous route information and improve the memory accuracy of the subsequent route information (Ma, Li, Jia, & Wei, 2022). However, for schizophrenia patients with impaired spatial location memory who have difficulty suppressing interference information, it is unknown whether the preposed tests can help them suppress proactive interference in route learning and thus improve the learning of subsequent information. Hence, this study potentially offers significant practical insights for the rehabilitation training of patients with schizophrenia.

Route learning can be processed using a two-dimensional planar map and a three-dimensional space (Carpenter et al., 2012; Rohrer et al., 2010; Li et al., 2015). A two-dimensional map is flat and smaller than the projected proportion of humans, and therefore, people can directly view the whole picture (so it refers to small-scale spatial information or both) (Montello, 1993). However, three-dimensional space is larger than the projected proportion of humans. For example, the space occupied by buildings, communities, campuses, and cities that we encounter in daily life refers to large-scale spatial information (Montello, 1993). With the development of virtual reality technology in recent years, space navigation in the real world can be simulated by constructing a virtual environment (Fouquet et al., 2010; Pine et al., 2002) whose search and visualization based on location information is more intuitive for realistic three-dimensional navigation (Rakkolainen et al., 2001). Compared with three-dimensional navigation, the learning of a two-dimensional map is simpler and faster because it emphasizes local features (such as landmarks) or global features (structural, such as city or regional boundaries), eliminates "unnecessary" content, and requires less cognitive resources, thus being more conducive to understanding. However, the learning of three-dimensional spatial routes, owing to its verisimilitude, contains more route background information and requires higher cognitive resources, but it is closer to real life. Therefore, the cognitive mechanisms of the two types of route learning are fundamentally different; however, each has its own advantages. This study will examine the respective forward testing effects in patients with schizophrenia when they learn two-dimensional or three-dimensional route information. On the one hand, we expect to examine the forward testing effects of route learning more comprehensively in patients with schizophrenia. More importantly, one of the mechanistic explanations for forward testing effects remains challenging as tests enhance learning by reducing distractions. Wissman et al. (2011) in their study, included a group with no prior material (no distractions) and found that learners who studied and took the mid-test had a significantly higher recall rate of the new material than the group without distractions. Because of the different spatial scales presented by the two types of route learning and different requirements for cognitive resources, the proactive interference, generated by the two-dimensional and the three-dimensional route information in the learning process, is also different. By comparing the two route learning outcomes, we can further reveal the internal mechanism of forward testing effects in the route learning of patients with schizophrenia.

In summary, the purpose of this study is to investigate the effect of forward testing on spatial route learning in patients with schizophrenia as compared to a healthy control group. Experiment 1 uses a two-dimensional planar route map to explore whether a pre-test can help schizophrenia patients suppress interference in learning and improve the ability of spatial location memory in two-dimensional planar maps. When compared with a two-dimensional planar map, the three-dimensional spatial route is closer to real life, which is helpful in identifying landmarks and finding routes in cities, thus leading patients to integrate into normal life after they re-enter society. Therefore, Experiment 2 utilizes 3D route information to further explore the forward testing effects in virtual spatial route learning in patients with schizophrenia. Additionally, as the sequence of landmarks is a fundamental dimension of the route memory (Allen, 2000), marked objects along the route are treated as landmarks and aid participants in acquiring spatial information by providing clues for identification and memory (Roser, HamBurger, Krumnack, & Knauff, 2012). In the present study, we regard the correct recall rate (for sequences of road signs) as the dependent variable. We hypothesize that, regardless of route learning in a 2D map or 3D virtual space, forward tests would be more helpful than repetitive learning for patients with schizophrenia in reducing the proactive interference of spatial information and improving the retention of subsequent new information.

Experiment 1: Forward Testing Effects in 2D Planar Route Map Learning in Schizophrenia

Method

Participants.

Based on the median of the range of effect sizes (Cohen's ds) for the forward testing effect observed by Yang et al. (2017) and with a statistical test power of $(1-\beta) = 0.80$, an efficacy analysis using G*Power 3 found that observing a significant forward testing effect (Faul, Erdfelder, Lang, & Buchner, 2007) required approximately 18–23 participants per group. Therefore, 128 participants (64 each in the healthy group and 64 in the schizophrenic group) were selected for Experiment 1. All participants were randomly assigned to the test and restudy groups, with 32 participants per group. They all signed an informed consent form. The inclusion criteria for patients with schizophrenia were: (1) meeting the DSM-5 diagnostic criteria for schizophrenia; (2) Age [?]18 years old; (3) Can understand the test content, can cooperate with the completion of the cognitive test; (4) Receive antipsychotic drug therapy: selected patients all received stable level of drug therapy and were able to understand the test requirements and cooperate with the completion of various research contents in the stable stage of disease treatment; (5) No history of neurological disease or another serious physical disease, no Intellectual Disability; (6) No alcohol or drug abuse, no history of electroshock, no family history of neurological diseases; (7) No color blindness, color weakness, and other color vision disorders, and normal or corrected vision. Exclusion criteria were as follows: (1) Having cognitive impairment caused by definite somatic or organic brain lesions, such as cerebrovascular disease, and brain trauma, among others; (2) Having a co-morbid diagnosis of depression; (3) Being diagnosed with mental disorders caused by substance dependence or abuse or use of psychoactive substances; (4) Having experienced a previous brain injury or other organic diseases related to the central nervous system; (5) Having a clear risk of suicide or harm to others. Each participant was provided a souvenir at the end of the experiment.

Experimental design.

This experiment used a 2 (group: healthy group or schizophrenia group) \times 2 (learning condition: test or restudy) between-subjects design. The rate of correct final recall and proactive interference were selected as dependent variables.

Instruments and materials.

The materials used the professional drawing software Procreate as a mapping tool with a certain urban district as the background and four different black-and-white road maps (Fig.1A). The route information included sketch maps of eight common landmark buildings: kindergartens, gymnasiums, swimming pools, hospitals, banks, convenience stores, restaurants, and parking lots (as shown in Fig.1). All patients with schizophrenia were assessed using the Attentional Control Scale, Executive Function Scale, Hamilton Anxiety Scale, Montreal Cognitive Assessment Scale, PANSS, Wechsler Intelligence Scale, and Wechsler Memory Scale. Only the Attention control, Executive function, and Hamilton anxiety scales were used for healthy participants.

Attentional Control Scale (ACS) : A 20-item scale with two dimensions representing the two aspects of attention control ability, namely, attention focus ability (to keep attention to one stimulus) and attention diversion ability (referring to the transfer of attention from one stimulus to another). The concentration of attention included 9 items and the transfer of attention included 11 items. The higher the score, the better the attention control ability.

Adult Executive Functioning Inventory (ADEXI) : The question adopts a reverse scoring method; the higher the score, the worse the performance of the corresponding component of executive function. The total score of working memory (the sum of scores of items 1, 2, 5, 7, 8, 9, 11, 12, and 13) and inhibition (the sum of scores of items 3, 4, 6, 10, and 14), and the total score of ADEXI is added together.

Hamilton Anxiety Scale (HAMA) : A 5-point scale with 14 items. The total score on the scale was used to evaluate the severity of patients' anxiety symptoms and the clinical treatment effect. The higher the score, the more severe the anxiety, and a score of less than 7 indicates no anxiety symptoms.

Montreal Cognitive Assessment Scale (MoCA, Beijing Edition) : An assessment tool for the rapid screening of cognitive abnormalities. There were 11 tests in eight cognitive areas, including attention and concentration, memory, language, abstract thinking, calculation, and orientation. The total score is 30; a

score of >26 is considered normal.

Positive and Negative Syndrome Scale (PANSS): This scale is primarily used to assess the severity of the main symptoms of schizophrenia treatment (such as positive and negative symptoms). The scale consisted of seven items on the positive scale, seven items on the negative scale, 16 items on the general psychiatric scale, and three supplementary items, which were used to assess the risk of aggression. Each item was rated on a scale of one to seven. Symptom assessment in patients with schizophrenia is performed by at least two specialized psychiatrists. Patients were assigned to the positive subtype if there were three or more items rated as moderate on the negative symptom scale but less than three items rated as moderate on the positive scale, they were classified as the negative subtype. Patients with at least three items rated as moderate on both scales were classified as mixed.

Wechsler Intelligence Scale (WIS) : This is composed of verbal intelligence, performance intelligence, and full-scale intelligence. The raw score (or rough score) of a subscale is the sum of the scores of the items in the subtest. When a subscale is missing, the weighted score is calculated. The original score can be converted into a scale score with an average of 10 and a standard deviation of 3 according to the table above. Verbal and performance scale scores are obtained by adding the scale scores of the verbal and performance tests. When the two are added, a full-scale score is obtained. Finally, the corresponding table is converted to verbal IQ, performance IQ, and full-scale IQ.

Wechsler Memory Scale (WMS) : This scale consists of seven subscales: general knowledge, orientation, mental control, logical memory, number span, visual memory, and word association learning. A memory quotient (MQ) is obtained by combining the scores of the seven items. The scale provides a very useful objective test method for clinical diagnosis and helps distinguish between organic and functional memory disorders.

The experimental material was presented on a 14-inch laptop screen $(1920 \times 1080 \text{ resolution})$ with brightness and contrast to avoid discomfort. The participants were approximately 60 cm away from the display facing each other. SPSS 27.0 was used for the data processing of all the experimental results.



Fig.1. Example of a building.













Experimental procedure.

Before the experiment started, participants were randomly assigned to two groups (test and restudy). Under these two groups and learning conditions, participants learned four plane route maps, including eight landmarks with four different directions. They were instructed to remember the locations of landmarks in each plane route map before the upcoming memory test. Each of the four plane route maps was presented for 60 seconds, followed by a 30-second distraction task. Under the repeated learning condition, each plane route map was presented for 60 seconds, and the participants were required to re-learn the plane route map. Under the test conditions, the E-prime program was used to present pictures of buildings to the healthy group—the participants pressed keys to select the order of the buildings. However, schizophrenic patients are often unfamiliar with computer keys and have compromised capability for fine movement of fingers. To reduce the difficulty of computer key operation, schizophrenic patients were provided with paper-based architectural pictures of landmark building routes and were asked to recall the order of the landmarks on the plane route map just presented. This method can reduce the decrease in spatial navigation performance caused by schizophrenia due to allocating too much attention resources to the fine movements of the fingers. After learning plane route map 4 and following the 30-second distraction, the test and relearning conditions were tested using plane route map 4.

Table 1 Experiment 1 Procedure (Routes 1-4)

Groups	Route 1	Route 2&3	Route 4
test group	study-distraction-test		study-distraction-test
restudy group	study-distraction-restudy		study-distraction-test

Results

The scores: the recall stage was scored by the experimental assistant. A point was scored for each correctly recalled landmark, and eight points were scored for each correct route. Participants' correct recall of each route was used to calculate an overall recall rate. The proactive interference rate of the participants' false recall of previous information in the current recall task was calculated. The proactive interference rate refers to the rate at which the subjects recall the order of buildings in the previous route information when recalling the current route information (for example, the order of buildings in Route 1 is A-B-C, and the correct order of buildings in Route 2 is C-A-B). When the participants recall the order of Route 2, the wrong recall is C-B-A, and B is the second building in Route 1, so B is the interference from Route 1. That is, if the subjects mistakenly placed the correct order of a building in Route 1 in the same position in Route 2, but everything else is correct, the interference rate is 1/8 = 0.125. If the information of the previous route is not in the same place as the building, or the order is simply confused, it is considered a recall error.

Participant characteristics of the 2D route map.

Table 2 Participant characteristics of the 2D route map

	Schizophrenia patients $(n=60)$	Schizophrenia patients $(n=60)$	Healthy controls $(n=60)$
Characteristic	M(SD);range	n(%)	M(SD);range
Female		26(43)	
Male		34(57)	
Age (years)	34.45(10.22);18-56		29.53(12.03);18-56
Attentional Control Scale	49.97(6.27);40-70		52.10(6.38);34-69
ADEXI	41.12(7.59);30-63		46.50(9.42);29-67
HAMA	5.55(6.51);0-40		7.62(5.48);0-19
Time since disease(months)	78.58(61.52);0.1-312		
Montreal Cognitive Assessment	19.28(6.15);4-29		

PANSS positive	10.1(3.9);7-31
PANSS negative	10.53(4.62);7-30
PANSS general	22.8(8.74);16-68
PANSS total	43.43(15.72);30-129
WAIS Verbal IQ	80.3(11.75);55-111
WAIS Performance IQ	76.57(16.27); 36-105
WAIS Full scale IQ	76.7(14.23);43-102
WMS	75.18(25.76);2-104
BPRS	26.54(9.8);18-65

Note. ADEXI=Adult Executive Functioning Inventory. HAMA=Hamilton Anxiety Scale. PANSS=Positive and Negative Syndrome Scale. WA1S = Wechsler Adult Intelligence Scale. WMS=Wechsler memory scale. BPRS=Brief Psychiatric Rating Scale

Correct recall rate and interference rate of test group in 2D routes map 1 - 4.



Fig.2. Correct recall and interference rate in 2D planar routes map 1 - 4 for healthy controls and schizophrenic patients.

As shown in **Fig.2**, taking the correct recall rate of routes 1 - 4 in the test group as the dependent variable, a repeated measures ANOVA of 2 (group: healthy group, schizophrenic group) × 4 (Routes:1 - 4) was conducted. The results showed that the main effect of route information was not significant, F (3,186)=0.69, p = 0.56, $\eta_p^2 = 0.01$, and the main effect of the group was significant, F (1,62) = 24.92, p < 0.001, $\eta_p^2 = 0.29$. The correct recall rate of patients with schizophrenia (M = 0.45, SD = 0.22) was significantly lower than that of the healthy control group (M = 0.72, SD = 0.21). The interaction between the two factors was not significant, F (3,186)=1.37, p = 0.25, $\eta_p^2 = 0.02$.

A repeated measures ANOVA with 2 (group: healthy, schizophrenia) 3 (route information: 2-4) using the interference rate of routes 1 - 4 showed that the main effect of route information was significant, F (2,124)=10.25, p < 0.001, $\eta_p^2 = 0.14$. The edge difference of the interference rate between Route 1 (M = 0.09, SD = 0.12) and Route 2 (M = 0.14, SD = 0.18) is significant, p = 0.061, d = 0.33, 95%CI[-0.10, 0.002]. The interference rate of Route 3 (M = 0.21, SD = 0.20) is significantly higher than those of routes 1 and 2, p < 0.001, d = 0.71, 95%CI[0.06,0.16], p = 0.012, d = 0.37, 95%CI[0.02, 0.12].

The main effect of the group was significant, $F(1,62)=8.56, p=0.005, \eta_p^2=0.12$. The interference rate was significantly higher in patients with schizophrenia (M=0.19, SD=0.11) than in the healthy controls (M=0.10, SD=0.13). The interaction between the two factors was non-significant, $F(2,124)=0.11, p=0.89, \eta_p^2=0.002$.

Correct recall and interference rate of 2D plane route map 4.



Fig.3. Correct recall in healthy controls and schizophrenic group in 2D plane route map 4

To verify the forward test effect, with accuracy as the dependent variable, a 2 (group: schizophrenic group, healthy group) ×2 (learning condition: test, restudy) ANOVA was used to compare the recall rates of healthy and schizophrenic patients during restudy and test on route 4 (see Fig.3). The results demonstrate that the main effect was significant, F(1,124)=14.87, p < 0.001, $\eta_p^2=0.11$, and the correct response rate of healthy controls was significantly higher than that of patients with schizophrenia (0.47 vs 0.30). The main effect of the learning condition was significant, F(1,124)=67.66, p < 0.001, $\eta_p^2=0.35$, and the test group was significantly more correct than the healthy group (0.57 vs 0.20). The interaction between the two factors was non-significant, F(1,124)=3.24, p = 0.074, $\eta_p^2 = 0.03$.



Fig.4. Interference rates in 2D planar route map 4 for healthy controls and schizophrenic group

With the interference rate dependent variable, the 2 (group: schizophrenic group, healthy group) × 2 (learning condition: test, restudy) ANOVA was compared with the interference rate of healthy and schizophrenic patients; the main effect margin was significant, F(1,124) = 3.88, p = 0.051, $\eta_p^2 = 0.03$, and the interference rate of the healthy control group was significantly lower than that of the schizophrenia group (0.28 vs 0.36). The main effect of the learning condition was significant, F(1,124) = 36.19, p < 0.001, $\eta_p^2 = 0.23$, and the interference rate in the test group was significantly lower than that in the restudy group (0.21 vs 0.43). The interaction between the two factors was non-significant, F(1,124) = 0.39, p = 0.54, $\eta_p^2 = 0.00$.

Mediator of the interference rate of route 4 in 2D plane route learning.

To test whether the forward test effect in this experiment was due to the test inhibiting proactive interference, the learning condition was set as the independent variable, the rate of correctness as the dependent variable, and the interference rate as the mediation variable. The PROCESS4.1 plug-in of SPSS27.0, which refers to the bootstrap method proposed by Hayes, was used (Hayes, 2013). Model 4, with a sample size of 5000, was selected. At the 95% confidence interval, learning condition was used as the independent variable X (assigned as test group=1, restudy group=2), A4 accuracy was the dependent variable Y, and A4 interference rate was the mediation variable M.



Fig.5. Mediator of accuracy and interference rates in the 2D plane route map 4 for healthy controls

For healthy controls, the results of the bootstrap analysis indicated that the indirect effect of the mediation test did not contain 0(B = -0.182, SE = 0.049,95% CI = [-0.284,-0.095]). Moreover, after controlling for the a4 interference rate, the direct effect of the learning condition on a4 accuracy was significant, and the interval did not include 0 (B = -0.275, SE = 0.060,95% CI = [-0.395,-0.155]).



Fig.6. Mediator of accuracy and interference rates in 2D plane route map 4 for Schizophrenic patients' group.

For the schizophrenia group, the results of the bootstrap analysis indicated that the indirect effect of the mediation test did not contain 0(B = -0.140, SE = 0.046,95% CI = [-0.245, -0.061]). Moreover, after controlling for the mediation variable a4 interference rate, the direct effect of the independent variable learning condition on the dependent variable A4 accuracy was significant, and the interval did not include 0 (B = -0.153, SE = 0.060,95% CI = [-0.979, -0.401]).

Discussion

The results of Experiment 1 show that the landmark order test in the first three routes improved the subject's memory of the building location order for the fourth route. Additionally, because the inhibition ability of schizophrenia patients is impaired, their ability to suppress proactive interference and promote follow-up new information is worse than that of healthy participants. The recall rate of the healthy group was significantly higher for route information 4 than that of the schizophrenia group, and the interference rate was significantly lower than that of the schizophrenia group. The results also show that patients with schizophrenia have a forward test effect in 2D plane route learning, indicating that a pre-test during route information learning can help schizophrenia patients to suppress proactive interference. This result is consistent with previous results obtained for spatial memory in healthy subject populations regarding card and object locations (Postma, Morel, Slot, Oudman, & Kessels, 2018; Bufe & Aslan, 2018). The mediation test shows that in 2D route learning, the mediation effect of the interference rate is significant, and it is part of the mediation, whether it is the healthy group or schizophrenic patients. This shows that a reduction in the interference rate plays a role in improving the correct rate, but there are other factors as well.

Considering that people need to move around and navigate routes in real life, three-dimensional spatial route learning has more clinical application value and ecological validity. It can play a meaningful role in helping patients adapt to their normal lives. Therefore, in Experiment 2, 3D video route information was used to continue exploring the forward test effect in the route learning of schizophrenia patients.

Experiment 2: Forward Test Effects in 3D Visuospatial Route Information Learning in Patients with Schizophrenia

Methods

Participants.

Referring to the calculation method for the number of participants in Experiment 1, 120 participants were recruited for Experiment 2. Among them, 60 patients with schizophrenia in Lanzhou Third People's Hospital

participated in the experiment, and 60 healthy people were randomly assigned to either the test or reeducation groups, with 30 people in each group. They all signed an informed consent form. The inclusion criteria for patients with schizophrenia were the same as those used in Study 1. After the experiment, each participant received a souvenir.

Experimental design.

A between-group design of 2 (group: healthy group, schizophrenia group) \times 2 (learning condition: test, restudy) was used. The dependent variables were the correct rate of final recall and the proactive interference rate.

Instruments and Materials.

For a more realistic learning environment, SketchUp mapping software was used for modeling, followed by rendering and editing using Lumion software. The experimental task was implemented using a display computer simulation that presented 3D visuospatial background information, as shown in Fig.7.

The virtual environment was set in the residential neighborhood of a city, and common landmark buildings were selected, with route information containing eight elements similar to those used in Experiment 1. Buildings were sequentially presented to the participants in a virtual reality environment from a first-person perspective and with an open field of view, which facilitated the participants' judgments about their surroundings. The viewpoint in the video moved at a consistent rate, pausing for approximately 1 second when passing through each target building to ensure that the building was fully visible to the participant and to increase the realism of the visual experience. The neighborhood had four different entrances and exits that made up the four different routes. Participants had to learn each route presented to them in a separate video; these shared the same difficulty level. To avoid the duplication of the two adjacent routes and the duplication of the buildings in the front and back routes, one building of the four routes would not appear twice in the same location. Therefore, the order of route presentation was fixed. The angle of the building presented during testing was the same as that used in the learning material because participants were better able to identify the scene when tested at the same angle (Shelton & McNamara, 2001).



Fig.7. Example of a building.



Fig.7A: ABCD represents Routes 1-4

Experimental procedures.

Same as in Experiment 1.

Results

Participant characteristic map of 3D video route information.

Table 3 Participant characteristic map of 3D video route information

	Schizophrenia patients $(n=60)$	Schizophrenia patients $(n=60)$	Healthy controls $(n=60)$
Characteristic	M(SD);range	n(%)	M(SD);range
Female		26(43)	
Male		34(57)	
Age (years)	34.45(10.22);18-56		29.53(12.03);18-56
Attentional Control Scale	49.97(6.27);40-70		52.10(6.38);34-69
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and Negative Syndrome Scale. WA1S = Wechsler Adult Intelligence Scale. WMS=Wechsler memory scale. BPRS=Brief Psychiatric Rating Scale

Correct recall rate and interference rate of the test group in 3D video route information 1 - 4.



Fig.8. Correct recall and interference rate in 3D video route information 1 - 4 for healthy controls and schizophrenia patients

As shown in Fig.8, the rate of correct route recall 1 - 4 in the test group was set as the dependent variable, and a repeated measures 2 (Group: healthy group, schizophrenic group) × 4 (Routes:1 - 4) ANOVA was conducted. Results demonstrate that the main effect of route information was significant, F (3,174)=5.15, p = 0.002, $\eta_p^2 = 0.08$. Further post-hoc testing showed that the correct recall rate of Route 1 (M = 0.60, SD = 0.28) was significantly higher than that of Route 2 (M = 0.45, SD = 0.28) and Route 3 (M = 0.49, SD = 0.31), p = 0.003, d = 0.54, 95%CI[0.05, 0.23], p = 0.02, d = 0.37, 95%CI[0.02, 0.20]. There was no significant difference in correct recall between Routes 1 and 4 (M = 0.58, SD = 0.32), p = 0.75, d = 0.07, 95%CI[-0.08, 0.10]), nor between routes 2 and 3, p = 0.41, d = 0.13, 95%CI[-0.11, 0.05]. The correct recall rate for Route

4 was significantly higher than those for Routes 2 and 3, p = 0.002, d = 0.43, 95%CI[0.05, 0.21], p = 0.03, d = 0.28, 95%CI[0.01, 0.18].

The main effect of the group on the recall rate was significant, F(1,58)=28.55, p < 0.001, $\eta_p^2=0.33$. The correct recall rate was significantly lower for the schizophrenia group (M = 0.41, SD = 0.18) than that of the healthy group (M = 0.65, SD = 0.17). There was also a significant interaction effect between group and route information, F(3,174)=3.88, p = 0.01, $\eta_p^2=0.06$. A simple-effects analysis demonstrates that for the healthy group there was no significant difference in the accuracy between Route 1 (M = 0.64, SD = 0.28), Route 2 (M = 0.56, SD = 0.28), and between Route 3(M = 0.63, SD = 0.32), p = 0.23, d = 0.31, 95%CI[-0.05, 0.21], p = 0.24, d = 0.03, 95%CI[-0.21, 0.05], p = 0.85, d = 0.23, 95%CI[-0.14, 0.12]. Route 4 (M = 0.77, SD = 0.26), and the correct rate of Route 1, 2, and 3, respectively, p = 0.05, d = 0.50, 95%CI[0.002, 0.26], p = 0.001, d = 0.81, 95%CI[0.10, 0.32], p = 0.03, d = 0.30, 95%CI[0.02, 0.27]. In the schizophrenia group, Route 1 (M = 0.55, SD = 0.28) had significantly higher accuracy than Route 2 (M = 0.35, SD = 0.24), Route 3 (M = 0.35, SD = 0.23), and Route 4, (M = 0.39, SD = 0.26, p = 0.003, d = 0.77, 95%CI[0.07, 0.34], p = 0.002, d = 0.77, 95%CI[0.08, 0.33], p = 0.016, d = 0.62, 95%CI[0.03, 0.29]. Differences in accuracy between Route 2, 3, and Route 4 were not significant, p = 1.000, d = 0.17, 95%CI[-0.11, 0.11], p = 0.46, d = 0, 95%CI[-0.17, 0.08], p = 0.42, d = 0.17, 95%CI[-0.16, 0.07].

A repeated measures ANOVA with 2 (group: healthy group or schizophrenic group) x 3 (Routes: 2-4) with the correct interference rate of route information 1 - 4 in the test group showed that the main effect of route information was not significant. F(2,116)=0.08, p=0.93, $\eta_p^2=0.001$. However, the main effect of the group was significant, F(1,58)=11.88, p=0.001, $\eta_p^2=0.17$, and the interference rate was significantly higher in

the schizophrenia group (M = 0.19, SD = 0.11) than in healthy controls (M = 0.10, SD = 0.09), p = 0.001, d = 0.90, 95% CI[0.04, 0.14]. There were no significant interactions between the two factors, F (2,116)=0.73, $p = 0.49, \eta_p^2 = 0.04$.

Correct recall rate and interference rate of 3D video route information 4.



Fig.9. Correct recall of healthy controls and schizophrenic patients in 3D video route information 4

To verify the forward test effect with the accuracy rate as the dependent variable, an analysis of variance of 2 (group: schizophrenic group, healthy group) × 2 (learning condition: test, restudy) was used. The results showed that the main effect of groups was significant, F(1,116)=56.16, p ;0.001, $\eta_p^2=0.33$. The healthy group was significantly more correct than the schizophrenia group (0.62 vs 0.27). The main effect of the learning condition was significant on the rate of correct responses, F(1,116)=33.63, p ;0.001, $\eta_p^2=0.23$. This was significantly higher in the test group than in the restudy group (0.58 vs 0.31). There was no interaction between the two factors, $F(1,116)=0.39, p=0.53, \eta_p^2=0.00$.



Fig.10. Interference rate in 3D video route information 4 for healthy controls and schizophrenic patients.

With interference rate set as a dependent variable, a 2 (group: schizophrenic group, healthy group) × 2 (learning condition: test, restudy) ANOVA demonstrated that its main effect was significant, F(1,116)=18.90, $p \ i0.001$, $\eta_p^2 = 0.14$. The interference rate of the healthy group was significantly lower than that of the schizophrenia group (0.18 vs 0.31). The main effect of the learning condition was also significant, F(1,116)=39.62, $p \ i0.001$, $\eta_p^2 = 0.26$. Whereby the interference rate in the test group was significantly lower than that in the restudy group (0.14 vs 0.35). The interaction between the group and learning conditions was not significant, F(1,124) = 0.71, p = 0.40, $\eta_p^2 = 0.00$.

Mediating effect of interference rate of route 4 in 3D video route learning.



Fig.11. Mediation of accuracy and interference rate in healthy controls in the 3D plane route map 4

For the healthy group, the results of the bootstrap analysis indicated that the indirect effect of the mediation test did not contain 0(B = -0.224, SE = 0.046, 95% CI = [-0.312, -0.128]). Moreover, after controlling for the mediation variable (a4 interference rate), the learning condition had a significant direct effect on a4 accuracy, and the interval did not include 0 (B = -0.076, SE = 0.055, 95% CI = [-0.187, 0.035]). For the schizophrenia group, the results of the bootstrap analysis indicated that the indirect effect of the mediation test did not

contain 0 (B = -0.122, SE = 0.046, 95% CI = [-0.225, -0.047]). Moreover, after controlling for the mediation variable A4 interference rate, the direct effect of the independent variable learning condition on A4 accuracy was significant, and the interval did not include 0 (B = -0.120, SE = 0.060, 95% CI = [-0.241, 0.000]).



Fig.12. Mediation of accuracy and interference rate in 3D plane route map 4 for the schizophrenia patient group.

Discussion

Experiment 2 verified the forward test effect on schizophrenic patients when learning 3D video route information. During the entire experiment, it was necessary to memorize the order of the buildings from different perspectives, and the route was not repeated. Compared with Experiment 1, the difficulty of memorizing increased. Therefore, the correct recall rate of the test group did not fluctuate with the increase in the number of tests. Moreover, because the inhibition ability of schizophrenia patients is impaired, their ability to resist proactive interference and promote subsequent new information is worse than that of healthy people, so the interference rate gradually increased. However, the interference rate of healthy individuals showed a downward trend. On route information 4, the effect of the forward test in patients with schizophrenia and healthy people was still verified. The correct recall rate of the test group for route information 4 was significantly higher than that of the restudy group, and the proactive interference in route information 4 was lower under the test condition than that under the restudy condition, which indicates that the test of route information 1-3 reduces the possibility that these previously learned materials will interfere with the recall of target material route information 4 compared with the restudy. Under the restudy condition, the memory of target route information 4 is worse than that of route information 1 under the test condition (no interference), which indicates that the interference increases with the number of repeated learning cycles. The results of the mediation test demonstrate that the mediation effect of the interference rate is significant and complete in 3D route learning, whether it is healthy or schizophrenic, which indicates that the reduction in the interference rate improves the correct rate. In this experiment, the forward test effect was based on the inhibition of proactive interference by the forward test.

General discussion

This study is the first to use learning materials such as planar maps and virtual communities to investigate the forward testing effects of schizophrenic patients in the learning of visuospatial route information. The results indicated that both patients with schizophrenia and healthy controls had enhanced recall rates. Consistent with previous findings in healthy individuals and patients with TBI (Szpunar et al., 2008; Pastötter et al., 2013), the research found that immediate tests of previously learned materials could reduce the intrusion of previously tested materials and then improve immediate recall of subsequent information (route information 4). This indicates that the effects of forward tests were not only limited to healthy individuals of all ages (Pastötter & Buml, 2019; Wang & Yang, 2020; Aslan, 2016; Yang, Sun, Potts, Yu, & Shanks, 2020) and

patients with traumatic brain injury (Pastötter et al., 2013), but could also be extended to the group of schizophrenia patients with inhibition defects, promoting the clinical application of forward testing effects in patients with cognitive impairments.

Specifically, in the learning of both the 2D spatial route (Experiment 1) and 3D (Experiment 2), the schizophrenia group, for routes 1–4 under the test condition, had lower immediate recall rates and higher interference rates than the healthy control group, indicating that compared with the healthy control group, schizophrenia patients generally showed impaired memory and more difficulty in suppressing distractions (Soriano, Jiménez, Román, & Bajo, 2009;Ullsperger, 2005;Davidson & Heinrichs, 2003). Nevertheless, in route 4, compared with repetitive learning, tests significantly enhanced memory retrieval in patients with schizophrenia, who suppressed proactive interference in the process of memory retrieval similar to the healthy control group. Therefore, this study fills this research gap by exploring whether forward testing effects play a role in spatial route learning in a group with cognitive impairments.

From the learning outcomes of routes 1 - 4 in the 3D virtual community, both the healthy and schizophrenia groups throughout the learning process of route information showed that accuracy rates decreased when interference rates increased or that the accuracy rate increased when the interference rate decreased. Many studies have indicated that forward-testing effects tend to be associated with a reduction in prior-list intrusion (Aslan, 2016; Bufe & Aslan, 2018; Yang, Chew, Sun, & Shanks, 2018). Specifically, these studies consistently observed that intermediate tests simultaneously enhanced the recall of new information and substantially reduced the number of previous-list information intrusions. A plausible inference is that there is a causal relationship between the reduction of previous-list information intrusion and the enhanced recall of new information; that is, intermediate tests enhance new learning by protecting it from proactive interference. By verifying the mediating effect of learning outcomes in Route 4, we found that the interference rate plays a fully mediating role between learning conditions and correct rates, which provides direct experimental evidence for the proactive interference hypothesis. This is consistent with the findings of a study in which researchers selected healthy college students as participants to explore their forward-testing effects in the learning of spatial route information (Ma, Li, Jia, & Wei, 2022).

The learning outcomes of individuals in routes 1 - 4 of the 2D map were slightly different from those of the 3D virtual community. The recall rates of the healthy subjects in the test group remained the same, and it was not the case that recall rates increased with more tests, while the interference rate decreased, but interference rates also increased slightly with more tests. Schizophrenia patients showed a slight increase with tests in recall rates of routes 1 - 4, but so did interference rates, possibly because the two-dimensional map was flat, and participants had an overall overview of the route when they learned the four maps with the same appearance only from different entrances. However, due to the high similarity of the four routes, they were more likely to be confused, and as a result, interference rates increased with increasing learning times. Under test conditions, the healthy and schizophrenia groups still had better recall rates and lower interference rates on the fourth route than under repetitive learning, further demonstrating the effects of forward testing. This suggests that the forward test was not only helpful in reducing interference but was also useful in promoting learning. Additionally, the mediating effect of the learning outcomes in Route 4 showed that interference rate plays a partial mediating role between learning conditions and accuracy rates. This suggests that in the learning of two-dimensional planar maps, the forward test may also bring benefits in ways other than inhibiting interference. This could be explained through the learning engagement (LE) theory to a certain extent, which states that the forward test recovers the reduction in learning participation during the learning cycle, leading to better learning of new information (Pastotter et al., 2011).

In this study, compared with three-dimensional navigation, the constructions in a two-dimensional background were conducive to simplifying the background from which people encoded and extracted targeted objects, and eliminating "unnecessary" interference stimuli in route learning, such as the color of green belts, residential buildings, and landmark buildings, contributing to low requirements for cognitive resources. As a result, the confidence and motivation of the participants in learning could be enhanced, which would improve route information memory. By integrating the results of the two experiments, this study suggests that observations of forward testing effects in schizophrenia patients' spatial route learning might be directly related to the reduction of proactive interference due to the forward test, and other mechanisms may also be involved. This implies that the "benefits" of the forward test may not be limited to reducing the interference. This study also focused on schizophrenia patients' ability to learn spatial route information and found that although the forward test could not completely inhibit the interference of previous contents on new information learned by patients, it significantly enhanced the effects of learning and remembering new information for schizophrenia patients. This memory paradigm effectively compensated for the deficiency caused by inhibition effects in schizophrenia patients since they were more susceptible to irrelevant interference. Thus, it is a powerful means to improve the learning and memory of patients with schizophrenia and has important application value in their cognitive rehabilitation training.

In conclusion, this study provides important new findings regarding how testing enhances visuospatial information learning in schizophrenia. It not only provides direct experimental evidence for the reduction of proactive inhibition theory but also finds that the benefits of testing are not limited to the reduction of proactive interference and that the requirements of learning materials on cognitive resources affected the mechanism of forward testing in promoting the learning of new information. However, this study has some limitations: we did not directly measure the cognitive load brought by the learning materials. Therefore, future research should consider cognitive load as the breakthrough point to explore deeply how learning materials and participants' memory features jointly act on the forward testing effect.

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