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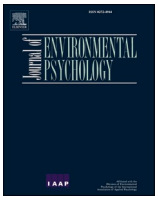

Route learning in patients with schizophrenia: The role of the forward testing effect

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ABSTRACT

Previous research demonstrated that practice testing on studied information can effectively potentiate subsequent learning of new information, a phenomenon known as the forward testing effect. However, it has never been explored whether practice testing can facilitate the efficiency of learning new information for patients with schizophrenia. The current study recruited 124 patients with schizophrenia and 124 healthy controls to explore the forward testing effect on learning of 2D planar route maps (Experiment 1) and 3D spatial route information (Experiment 2). Experiment 1 showed that, for both patients with schizophrenia and healthy control participants, interim testing substantially boosted subsequent learning and recall of 2D planar route maps. Experiment 2 further demonstrated that, by comparison with interim restudying, interim testing effectively facilitated subsequent learning and recall of 3D spatial routes. Furthermore, the results demonstrated that interim testing effectively prevented the build-up of proactive interference for patients with schizophrenia. The documented findings suggest that interim testing is an effective strategy to enhance learning and memory for patients with schizophrenia.

1. Introduction

During the process of memory retrieval, patients with schizophrenia exhibit inhibitory defects, making it challenging for them to suppress the interference caused by competing elements (Soriano et al., 2009). Additionally, it is difficult for them to inhibit intrusive or unwanted thoughts, ignore irrelevant targets, and inhibit dominant responses (Weisbrod et al., 2000). Waters et al. (2003) found evidence of an inhibitory defect in patients with schizophrenia when they were asked to inhibit irrelevant memories. This is a specific defect in patients with medial orbitofrontal lesions and cognitive impairment (Daniel et al., 2007). Impaired spatial cognitive function may be a more severe form of cognitive dysfunction in schizophrenia. For instance, in the backward masking task designed to assess visual processing channels alone, patients with schizophrenia showed deficits in spatial location but not in letter identification (Cadenhead et al., 1998). Besides, patients were more impaired in the location memory task than in the target recognition and relocation tasks (Danion et al., 1996).

Spatial memory plays a central role in everyday navigation and in supporting episodic memory, which is a key predictor of functional outcomes among patients with schizophrenia (Ranganath et al., 2008). Route learning is a type of spatial navigation that reflects an understanding of a specific route in the environment. It involves learning of route information from one location to another, usually consisting of a series of landmarks and movements from the start point to the destination (Siegel & White, 1975). Route memory stores information about the direction of intersections and the order of landmarks along the route (Nys et al., 2018). Patients with schizophrenia encounter greater challenges in recalling sequences of landmarks when retrieving previously navigated routes, indicating an impairment in their temporal memory for routes, while their visual memory for identifying landmarks remains unaffected (Daniel et al., 2007; Fraser, 2004).

Memory rehabilitation therapy proposes that effective learning strategies are needed to improve the normal life of patients with cognitive impairments during and after their recovery (Medalia et al., 2001; Patterson et al., 2022; van der Gaag et al., 2002), including free

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recall tests, recall 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 effectiveness of interim testing for improving learning and memory in healthy individuals and clinical patients (Pastötter et al., 2013).

Testing information after initial learning has been shown to aid in the encoding and retrieval of new information compared to restudying or doing nothing, as demonstrated by numerous studies (Pastötter & Bäuml, 2014; Yang et al., 2018). Following prior studies (Pastötter et al., 2013; Yang et al., 2018), we term the prospective benefits of interim testing on new learning as the forward testing effect (FTE). The FTE is typically investigated by using a multi-list or multi-section learning paradigm. For example, participants are asked to memorize five lists of words. For Lists 1–4, participants in the test condition take a recall test after studying each list, while those in the control condition are not tested. Then participants in both conditions study List 5 and take a test on it. The difference in List 5 recall between the two conditions represents the influence of interim testing on new learning (Szpunar et al., 2008). The FTE is observed when participants in the test condition successfully recall more List 5 words than those in the no-test condition (Dang et al., 2021). Proactive interference (PI) is widely recognized as a major source of forgetting (Kliegl & Bäuml, 2021), and Szpunar et al. (2008) argued that interim testing can effectively reduce the build-up of PI and facilitate learning and recall of List 5 words (target information). Put differently, interim tests improve the distinction and discrimination between lists, which then allows individuals to better distinguish specific information among lists, reduces PI, and improves recall of new information (Kliegl & Bäuml, 2021; Yang et al., 2019). Szpunar et al. (2008) termed this explanation as the release from PI theory.

Previous studies have shown that for healthy adults, interim testing can effectively reduce interference from previous route information and improve learning and recall of new routes, reflecting a FTE on memory for spatial position information (Ma et al., 2022). Apart from healthy adults, the FTE can also be generalized to patients with severe Traumatic brain injury (Pastötter et al., 2013). Does interim testing aid in improving memory for landmark positions in new routes for patients with schizophrenia who struggle to inhibit interfering information and have difficulty remembering spatial information? This is the issue that the present study aims to delve into. Addressing this question holds significant practical implications for the rehabilitation training of patients with schizophrenia. Additionally, regarding the mechanistic of the FTE, the interpretation that interim testing enhances learning by reducing PI remains challenged. This study focuses on individuals with impaired inhibitory abilities due to schizophrenia and investigates the release from PI theory during route learning. This exploration will further elucidate the underlying mechanisms of the FTE.

The current research employs two spatial background presentation formats: two-dimensional (2D) planar maps and three-dimensional (3D) spatial backgrounds. The 2D map is plane, provides a comprehensive view of the route, and falls under the category of small-scale spatial information. On the other hand, 3D map represents the spatial dimensions encountered in daily life, such as buildings, communities, campuses, and cities, constituting large-scale spatial information (Montello, 1993). Compared to the dynamic presentation of 3D spatial backgrounds, the buildings in 2D planar maps exhibit more monotony in color and structure. Consequently, when learning routes, participants demonstrate a better grasp of the building information along the entire route. 3D spatial backgrounds involve dynamic presentations, with buildings appearing sequentially. This format tests participants' encoding and processing of the sequence in which buildings appear, requiring higher levels of cognitive resources. However, it aligns more closely with real-life scenarios (Courbois et al., 2019; Löwen et al., 2019). Therefore, the cognitive mechanisms underlying the two types of route learning are fundamentally different. However, each has its advantages. The current study aims to examine the FTE in patients with schizophrenia on their learning of 2D or 3D route information. On the one hand, we aim to examine the FTE of route learning more comprehensively in patients with schizophrenia. More importantly, because of the different spatial scales presented by the two types of route learning and different requirements of cognitive resources, the PI generated by the 2D and the 3D routes in the learning process is also different. By comparing the two route learning outcomes, we can further examine the internal mechanisms underlying the FTE on route learning for patients with schizophrenia.

In summary, the current study aims to investigate the FTE on spatial route learning for patients with schizophrenia and healthy controls. Experiment 1 employed a 2D route map to explore whether interim testing can help patients with schizophrenia reduce PI and improve spatial position memory for a 2D map. Furthermore, given that 3D spatial route learning is closer to real-life situations, and that using 3D can help identify landmarks and find routes in cities, it can better assist patients in reintegrating into normal life after treatment. Therefore, in Experiment 2, we used 3D routes to further investigate the FTE in virtual spatial route learning in patients with schizophrenia.

2. Experiment 1: The forward testing effect on 2D map learning for patients with schizophrenia

2.1. Method

2.1.1. Participants

Based on median effect sizes (Cohen's *d*) of the FTE, a power analysis conducted via G*Power 3 showed that approximately 18–23 participants per group were required to observe a significant FTE with a statistical test power of $(1\text{-}\beta) = 0.80$ (Faul et al., 2007; Yang et al., 2017). Thus, a total of 128 participated in this experiment. Of these, 64 healthy adults ($M = 27.52$ years old, $SD = 10.16$; 16 females) and 64 patients with schizophrenia ($M = 36.25$ years old, $SD = 9.54$; 34 females) were recruited. All participants were randomly assigned to the test and restudy groups, with 32 participants per group.

The healthy groups were recruited through advertisements, had normal visual acuity or corrected vision, and reported no history of psychiatric illness in themselves or close family members. For patients with schizophrenia, the diagnosis was based on two psychiatrists. All participants signed a written informed consent. The study was approved by the Ethics Committee of the Third People's Hospital of Lanzhou City (Lanzhou Mental Health Center-Psychiatry Rehabilitation Sanatorium) and the School of Psychology of Northwest Normal University.

Inclusion criteria for patients with schizophrenia were as follows: (1) Based on the criteria of the *Diagnostic and Statistical Manual of the American Psychiatric Association (DSM–5)*; (2) age $\geq$18 years, regardless of gender; (3) all patients receiving stable antipsychotic medication treatment, in a stable phase of illness, able to understand testing requirements, and cooperate to complete all study tasks; (4) no history of neurological or other severe physical diseases, no mental retardation; (5) no color blindness, color weakness, normal vision, or corrected vision.

Exclusion criteria encompassed individuals with (1) cognitive impairments attributed to structural or organic lesions in the body, such as cerebrovascular diseases or traumatic brain injuries; (2) comorbid depression; (3) psychiatric disorders resulting from substance dependence or abuse of psychoactive substances; (4) a history of previous brain injury or other central nervous system-related organic diseases; (5) evident risk of self-harm or harm to others.

Several questionnaires were implemented. Demographic information and neuropsychological test scores are provided in Table 1. See the Supplementary Materials (SM) for details of these scales.

2.1.2. Design

This experiment used a 2 (Group: healthy controls vs. patients with

Table 1
Group demographics.

Characteristic	Patients with schizophrenia (n = 64)	Healthy controls (n = 64)		
	M (SD); range	M (SD); range	p	Cohen's d
Age (years)	36.25 (9.54); 20 - 54	27.52 (10.16); 18 - 54	0	0.88
Attentional Control Scale	52.79 (7.84); 40 - 71	49.34 (3.90); 38 - 57	0.002	0.55
ADEXI	42.17 (10.04); 19 - 69	44.13 (5.79); 32 - 59	0.18	0.24
HAMA	8.44 (4.48); 0 - 16	23.06 (7.58); 13 - 52	0	2.33
Time since disease (months)	137.37 (106.72); 2 - 456			
Montreal Cognitive Assessment	20.16 (6.71); 3 - 30			
PANSS positive	11.36 (2.3); 7 - 14			
PANSS negative	11.1 (2.82); 7 - 21			
PANSS general	22.43 (6.21); 16 - 37			
PANSS total	45.39 (10.20); 30 - 65			
WAIS Verbal IQ	74.12 (17.22); 34 - 102			
WAIS Performance IQ	68.97 (24.29); 7 - 124			
WAIS Full-scale IQ	75.17 (16.66); 42 - 110			
WMS	72.81 (25.69); 2 - 114			
BPRS	29.78 (6.46); 18 - 54			

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.

schizophrenia) × 2 (Learning condition: test vs. restudy) between-subjects design. The rate of correct recall and PI were selected as dependent variables.

2.1.3. Materials

Using the digital drawing application Procreate as a drawing tool, we created eight simplified sketches of common buildings, namely a kindergarten, gym, swimming pool, hospital, bank, convenience store, restaurant, and parking lot. These buildings form a complete route resembling a community. Next, we established four distinct entrances, ultimately resulting in four routes with different sequences of buildings (see Fig. 1).

2.1.4. Procedure

The experimental materials were presented on a 14-inch laptop screen (1920 × 1080 resolution) with brightness and contrast to avoid discomfort. Participants were seated approximately 60 cm away from the display. They first received the following instructions: "*Next, the computer will present four planar road maps in turn, with each map presented for about 60 s. When you have finished learning each route, you need to spend 30 s solving a few math problems. After studying each route, the computer would randomly decide either to give you a memory test or to offer a restudy opportunity before moving on to the next route.*" In fact, the test decisions were predetermined, with the Test groups tested on each of Routes 1–4 and the Restudy groups restudying Routes1-3 before being tested on Route 4 (see Table 2).

Fig. 1a. Example of a building.

In the Route 1 study phase, a 2D planar map displaying building numbers (1–8) was presented for 60 s. After studying Route 1, both the Test and Restudy groups solved as many simple math problems (e.g., *22 + 9 = ?*) as they could for 30 s. Next, the Test groups were instructed to recall the correct sequence of buildings from the just-learned Route 1. The computer presented eight buildings with random letter codes (A-H), providing patients with schizophrenia with a response sheet to write down the correct order of buildings in the route by corresponding letter codes. The healthy group matched the building codes presented to patients with schizophrenia and selected the correct sequence of buildings accordingly. Since reaction times were not recorded, this method did not affect the data results. During all interim testing periods, participants had unlimited time to recall the sequence of the route until completion, and then they proceeded to learn the next route. The restudy groups underwent another 60-s session of learning the 2D planar map of Route 1. The procedures for Routes 2–3 were the same as for Route 1, except that the participants studied a new order of buildings in each route.

After the completion of Route 3, both groups studied Route 4 and solved math problems for 30 s. Then the Test and Restudy groups were informed that the computer had decided to test them on Route 4 (i.e., they will be asked to recall the order in which the buildings appear in the route). Next, all participants completed the interim test on Route 4.

2.2. Results

SPSS 27.0 was used for analyzing all the experimental results. Scores were assigned by experiment assistants, with 1 point awarded for each correctly recalled building's sequence in a route, totaling 8 points for each route. The correct recall rate was then calculated. Additionally, proactive interference scores (PI) were computed, representing the intrusion ratio of landmark sequences from previous routes when recalling the current route.

2.2.1. Correct recall rate and interference rate of the test groups across routes 1–4

As shown in Fig. 2a, taking correct recall rate of Routes 1–4 in the test groups as the dependent variable, a mixed ANOVA of 2 (Group: healthy controls vs. patients with schizophrenia) × 4 (Route: 1–4) was conducted. The results showed that the main effect of route was not significant, F (3, 186) = 0.69, p = 0.56, η_p^2 = 0.01. The main effect of the group was significant, F (1, 62) = 24.92, p < 0.001, η_p^2 = 0.29. The correct recall rate in the patient groups (M = 0.45, SD = 0.22) was significantly lower than that in the healthy control groups (M = 0.71, SD = 0.21). The interaction between the two factors was not significant, F (3, 186) = 1.37, p = 0.25, η_p^2 = 0.02.

A mixed ANOVA with 2 (Group: healthy controls vs. patients with schizophrenia) × 3 (Route: 2–4) with interference rate of Routes 2–4 showed that the main effect of the route was significant, F (2, 124) = 10.25, p < 0.001, η_p^2 = 0.14. The difference in the interference rate between Route 2 (M = 0.09, SD = 0.12) and Route 3 (M = 0.14, SD = 0.18) was not significant, p = 0.061, d = 0.33, 95%CI [−0.10, 0.002]. The interference rate of Route 4 (M = 0.21, SD = 0.20) is significantly higher than those of Route 2, p < 0.001, d = 0.71, 95%CI [0.06, 0.16], and Route 3, 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, η_p^2 = 0.12. The interference rate was significantly higher in patients with schizophrenia (M = 0.19, SD = 0.11) than in the healthy

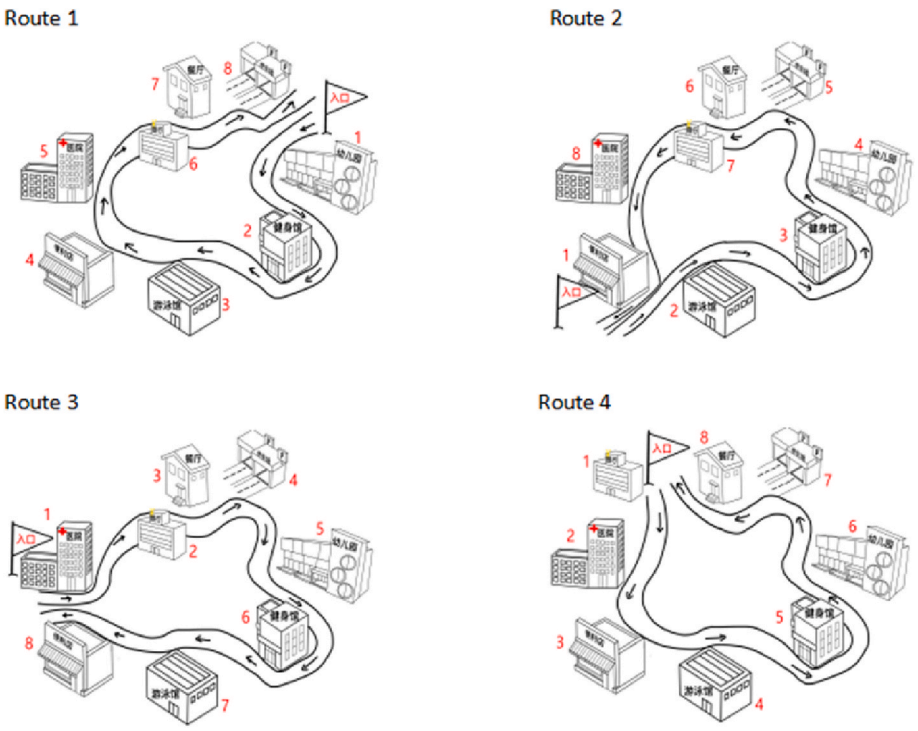

Fig. 1b. Routes 1-4.

Table 2
Experiment procedure of Experiment 1.

Groups	Routes 1-3	Route 4
Test	Study-distraction-test	Study-distraction-test
Restudy	Study-distraction-restudy	Study-distraction-test

controls ($M = 0.10$, $SD = 0.13$). The interaction between the two factors was non-significant, F (2, 124) = 0.11, $p = 0.89$, $\eta_p^2 = 0.002$.

2.2.2. Correct recall and interference rate of route 4

To verify the FET, with accuracy as the dependent variable, a 2 (Group: healthy controls vs. patients with schizophrenia) × 2 (Learning condition: test vs. restudy) ANOVA was used to compare the recall rates in healthy and patients with schizophrenia during the interim test on Route 4 (see Fig. 2b). The results showed a significant main effect of group, F (1, 124) = 14.87, $p < 0.001$, $\eta_p^2 = 0.11$, with a significantly higher rate of correctness in the healthy control group ($M = 0.47$, $SD = 0.36$) than in the patients with schizophrenia ($M = 0.30$, $SD = 0.28$), t (126) = 3.10, $p < 0.001$, $d = 0.52$, 95%CI [0.06, 0.29]. There was a significant main effect of learning condition, F (1, 124) = 67.66, $p < 0.001$, $\eta_p^2 = 0.35$, with the test group having a significantly higher rate of correctness ($M = 0.57$, $SD = 0.34$) than the restudy group ($M = 0.20$, $SD = 0.19$), t (126) = 7.75, $p < 0.001$, $d = 1.34$, 95%CI [0.28, 0.47]. The interaction between the two factors was non-significant, F (1, 124) = 3.24, $p = 0.074$, $\eta_p^2 = 0.03$.

The FET was examined separately for the patients with schizophrenia and the healthy controls. For the healthy controls, the results showed a significantly higher recall rate in the test ($M = 0.70$, $SD = 0.31$) than in the restudy group ($M = 0.25$, $SD = 0.23$), t (62) = 6.69, $p < 0.001$, $d = 1.65$, 95%CI [0.32, 0.59]. For patients with schizophrenia, the recall rate was also significantly higher in the test ($M = 0.45$, $SD = 0.31$) than in the restudy group ($M = 0.15$, $SD = 0.14$), t (62) = 4.85, $p < 0.001$, $d = 1.24$, 95%CI [0.17, 0.41]. Hence, a FTE was observed in both the healthy controls and patients with schizophrenia.

As shown in Fig. 2c, with the interference rate dependent variable, a 2 (Group: patients with schizophrenia vs. healthy controls) × 2 (Learning condition: test vs. restudy) ANOVA was conducted. The results showed a significant main effect of group, F (1, 124) = 3.88, $p = 0.051$, $\eta_p^2 = 0.03$, with the interference rate in the healthy controls ($M = 0.28$, $SD = 0.27$) significantly lower than that in patients with schizophrenia ($M = 0.36$, $SD = 0.21$). The main effect of learning condition was significant, F (1, 124) = 36.19, $p < 0.001$, $\eta_p^2 = 0.23$, with interference rate in the test groups ($M = 0.21$, $SD = 0.20$) significantly lower than that in the restudy groups ($M = 0.43$, $SD = 0.23$), t (126) = 5.96, $p < 0.001$, $d = 1.35$, 95%CI [0.15, 0.30]. The interaction between the two factors was non-significant, F (1, 124) = 0.39, $p = 0.54$, $\eta_p^2 = 0$.

Further, PI was tested separately for patients with schizophrenia and healthy controls. Results showed that, for the healthy controls, the interference rate in the test ($M = 0.16$, $SD = 0.21$) was significantly lower than that in the restudy condition ($M = 0.41$, $SD = 0.27$), t (62) = 4.17, $p < 0.001$, $d = 1.03$, 95%CI [0.13, 0.37]. For patients with schizophrenia, the test condition ($M = 0.25$, $SD = 0.18$) was significantly lower than that the restudy condition ($M = 0.46$, $SD = 0.19$), t (62) = 4.45, $p < 0.001$, $d = 0.14$, 95%CI [0.11, 0.29].

2.2.3. Mediation analyses

To examine whether the FET in this experiment is due to a reduction in PI, a mediation analysis was conducted with learning condition as the independent variable (coded as a dummy variable: test = 1; restudy = 0), Route 4 correct recall as the dependent variable, and proactive interference (PI) rate as the mediator. This mediation analysis was conducted via the SPSS *PROCESS* (Version 4.1) package, with a bootstrap sample set to 5000 (Montoya & Hayes, 2017).

For the healthy controls (Fig. 3a), the results indicated that the indirect effect of the mediation test did not contain 0 (*Effect* = 0.182, *SE* = 0.048, 95%CI [0.093, 0.282]), which accounted for 39.82 % of the total effect. Moreover, after controlling for the PI, the direct effect of the learning condition on R4 correct recall was significant, and the interval did not include 0 (*Effect* = 0.275, *SE* = 0.060, 95%CI [0.155, 0.395]).

For the patients with schizophrenia group (Fig. 3b), the results indicated that the indirect effect of the mediation test did not contain 0 (*Effect* = 0.140, *SE* = 0.047, 95%CI [0.061, 0.242]), which accounted

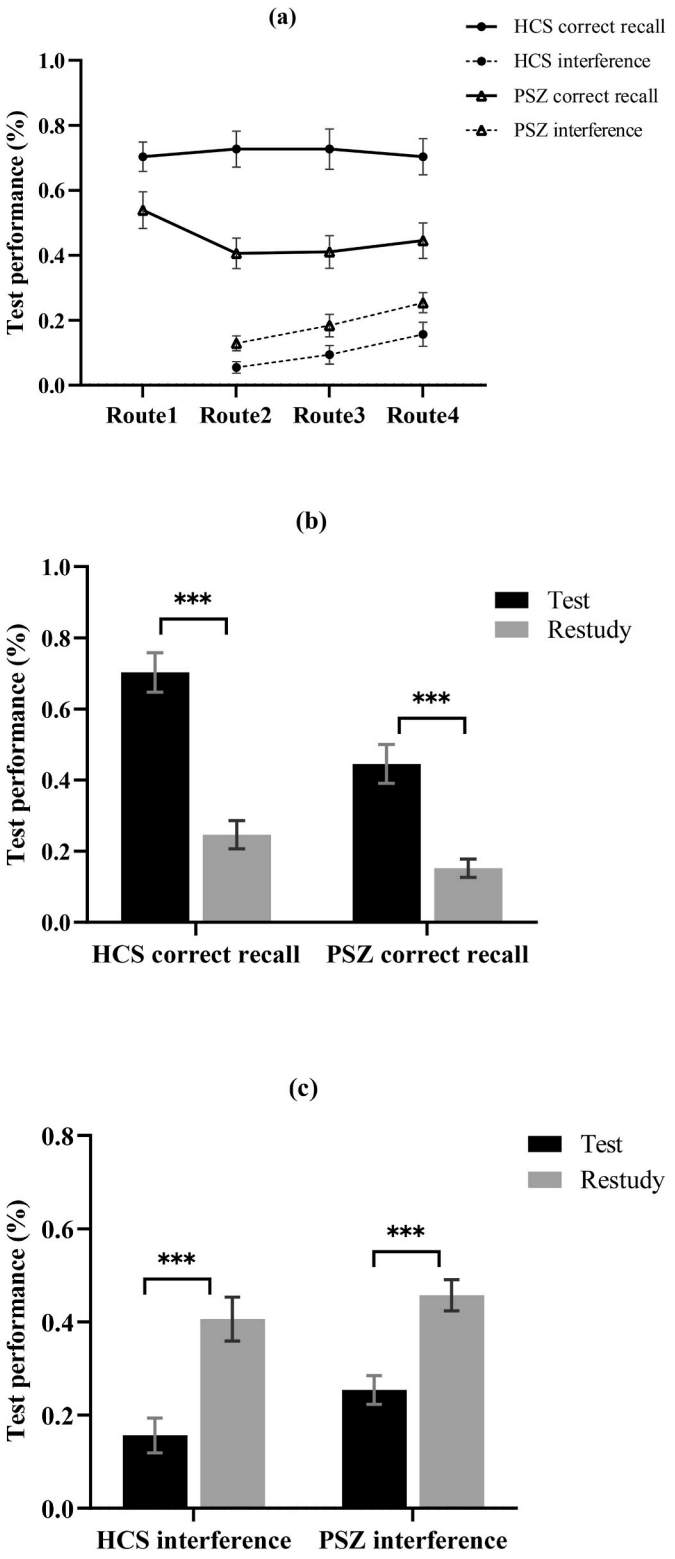

Fig. 2. (a) Correct recall and interference rate in Routes 1–4 for healthy controls (HCS) and patients with schizophrenia (PSZ). **(b)** Correct recall in healthy controls and patients with schizophrenia group in Route4. **(c)** Interference rates in healthy controls and patients with schizophrenia group in Route 4. ***$p < 0.001$; **$p < 0.01$; *$p < 0.05$.

for 47.82% of the total effect. Moreover, after controlling for the mediation variable PI, the direct effect of the independent variable learning condition on the dependent variable R4 correct recall was significant, and the interval did not include 0 (*Effect* = 0.153, *SE* = 0.060, 95%CI [0.034, 0.272]). In addition, we analyzed executive function and attention as mediating variables, and PANSS and IQ measurements as concomitant variables in the patient population, and found that none of them were significant (See SM for details).

To further compare the difference between patients with schizophrenia and healthy controls, the group was used as a moderator variable (patients with schizophrenia = 1, healthy controls = 0). Learning condition is the independent variable, R4 correct recall is the dependent variable, and PI is the mediating variable. Bootstrap analyses showed that there was no significant moderating effect of group in the effect of learning condition on PI ($p = 0.535$), suggesting that interim testing increased recall correctness through a reduction in PI in both patients with schizophrenia and healthy controls.

2.3. Discussion

Results from Experiment 1 indicated that testing landmark sequences in the first three routes improved participants' memory for landmark sequences in the fourth route. Significant FTE was observed in both healthy and schizophrenia patient groups. Due to impaired inhibitory abilities in schizophrenia patients, their performance in inhibiting PI and facilitating subsequent new information was poorer than that of the healthy group. Mediation analysis suggested that the reduction in interference rates partially mediated the improvement in recall accuracy.

Considering that route learning in a 3D background is more clinically applicable and ecologically valid, it can effectively help patients adapt to normal life. Experiment 2 utilized 3D video to continue exploring FTE for route learning in patients with schizophrenia.

3. Experiment 2: The forward testing effects on 3D spatial learning for patients with schizophrenia

3.1. Methods

3.1.1. Participants

Referring to the method of calculating the number of participants in Experiment 1, 120 participants were reselected for Experiment 2, including 60 ($M = 29.53$ years old, $SD = 12.03$; 45 females) in the healthy group, 60 patients with schizophrenia ($M = 34.45$ years old, $SD = 10.22$; 26 females) recruited from the Third People's Hospital of Lanzhou City. All participants signed an informed consent form. Inclusion criteria for patients with schizophrenia were the same as those required for Experiment 1. Demographic information and neuropsychological test scores are provided in Table 3.

3.1.2. Design

This experiment used a 2 (Group: healthy controls vs. patients with schizophrenia) × 2 (Learning condition: test vs. restudy) between-subjects design. The rate of correct recall and proactive interference were selected as dependent variables.

3.1.3. Materials

The same 8 buildings were used as in Experiment 1 (see Fig. 4). To reflect the realism of the learning environment, Sketchup mapping software was used for modeling and then rendered and edited in Lumion, resulting in 4 videos of 3D route information. The buildings in the routes were presented one by one in the virtual environment from a first-person perspective, with a wide field of view in the environment and a 1-s pause when passing each building to ensure that they could be seen clearly while increasing the realism of the visual experience. Each route was presented in a separate video, so participants had to learn a

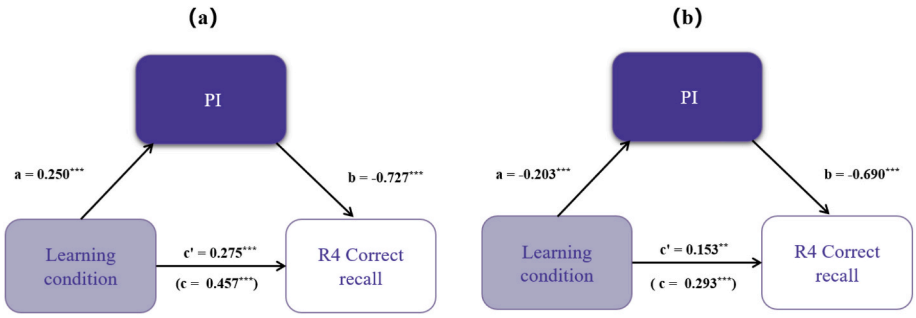

Fig. 3. Mediation model diagram between learning condition and correct recall of Route 4 (R4), where PI refers to proactive interference in Route 4. **(a)** Mediation model for the healthy control group. **(b)** Mediation model for patients with schizophrenia. ***$p < 0.001$; **$p < 0.01$; *$p < 0.05$.

Table 3
Group demographics.

Characteristic	Patients with schizophrenia (n = 60)	Healthy controls (n = 60)		
	M (SD); range	M (SD); range	p	Cohen's d
Age (years)	34.45 (10.22); 18 - 56	29.53 (12.03); 18 - 56	0.02	0.44
Attentional Control Scale	48.42 (6.41); 36 - 70	48.17 (5.43); 28 - 60	0.82	0.04
ADEXI	41.18 (6.26); 30 - 63	46.50 (9.42); 29 - 67	0	0.66
HAMA	5.55 (6.51); 0 - 40	7.62 (5.48); 0 - 19	0.062	0.34
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.

total of four different video routes. In addition, to avoid duplicating the order of buildings in two neighboring routes, it was ensured that a building would not appear twice in the same location in all four routes. Hence, the presentation sequence of Routes 1–4 remained constant.

3.1.4. Procedure

The phases of route learning and testing were identical to those of Experiment 1. The distinction lay in the fact that Experiment 2 had a video presentation of the route set against a 3D background, while Experiment 1 was a 2D planar map.

3.2. Results

3.2.1. Correct recall rate and interference rate of the test group in routes 1-4

As shown in Fig. 5 a, taking correct rate of Routes 1–4 in the test groups as the dependent variable, and a repeated measure 2 (Group: healthy controls vs. patients with schizophrenia) × 4 (Routes: 1–4)

Fig. 4a. Example of a building.

ANOVA was conducted. Results demonstrate that the main effect of Routes was significant. F (3, 174) = 5.15, $p = 0.002$, $\eta_p^2 = 0.08$. 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 ($M = 0.45$, $SD = 0.28$), $p = 0.003$, $d = 0.54$, 95%CI [0.05, 0.23], and Route 3 ($M = 0.49$, $SD = 0.31$), $p = 0.02$, $d = 0.37$, 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 Route 2, $p = 0.002$, $d = 0.43$, 95%CI [0.05, 0.21] and Route 3, $p = 0.04$, $d = 0.28$, 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 patients with schizophrenia ($M = 0.41$, $SD = 0.18$) than that of the healthy controls ($M = 0.65$, $SD = 0.17$). The interaction between the two factors was significant, F (3, 174) = 3.88, $p = 0.01$, $\eta_p^2 = 0.06$. A simple-effects analysis demonstrates that for the healthy controls group, there was no significant difference in the correct recall between Route 1 ($M = 0.64$, $SD = 0.28$) and Route 2 ($M = 0.56$, $SD = 0.28$), $p = 0.23$, $d = 0.31$, 95%CI [−0.05, 0.21], and Route 3 ($M = 0.63$, $SD = 0.32$), $p = 0.24$, $d = 0.03$, 95%CI [−0.21, 0.05], Route 2 and 3, $p = 0.85$, $d = 0.23$, 95%CI [−0.14, 0.12]. Correctness for Route 4 ($M = 0.77$, $SD = 0.26$) differed significantly from Route 1, $p = 0.05$, $d = 0.50$, 95% CI [0.002, 0.26], and Route 2, $p < 0.001$, $d = 0.81$, 95%CI [0.10, 0.32], and Route 3, $p = 0.03$, $d = 0.30$, 95%CI [0.02, 0.27] were both significantly different. In patients with schizophrenia, Route 1 ($M = 0.55$, $SD = 0.28$) had significantly higher correct recall than Route 2 ($M = 0.35$, $SD = 0.24$), $p = 0.001$, $d = 0.77$, 95%CI [0.09, 0.32], and Route 3 ($M = 0.35$, $SD = 0.23$), $p = 0.001$, $d = 0.77$, 95%CI [0.09, 0.32], and Route 4

Fig. 4b. Overhead view of Routes 1-4.

($M = 0.39$, $SD = 0.26$), $p = 0.004$, $d = 0.62$, 95%CI [0.06, 0.26]. Differences in correct recall between Route 2 and 3, $p = 1.000$, $d = 0$, 95% CI [−0.09, 0.09], and Route 4, $p = 0.40$, $d = 0.18$, 95%CI [−0.15, 0.06], Route 3 and 4, $p = 0.38$, $d = 0.19$, 95%CI [−0.15, 0.06] were not significant.

A repeated measures ANOVA with 2 (Group: healthy controls vs. patients with schizophrenia) × 3 (Routes: 2–4) with the 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 patients with 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, $p = 0.49$, $\eta_p^2 = 0.04$.

3.2.2. Correct recall and interference rate of route 4

To verify the FET, with accuracy as the dependent variable, a 2 (Group: healthy controls vs. patients with schizophrenia) × 2 (Learning condition: test vs. restudy) was used to compare the recall rates in healthy and patients with schizophrenia during the interim test on Route 4 (see Fig. 5b). There was a significant main effect of group, F (1, 116) = 56.16, $p < 0.001$, $\eta_p^2 = 0.33$, and the correct rate was significantly higher in healthy controls ($M = 0.62$, $SD = 0.32$) than in patients with schizophrenia ($M = 0.27$, $SD = 0.25$), t (118) = 6.65, $p < 0.001$, $d = 1.22$, 95%CI [0.25, 0.45]. There was a significant main effect of learning condition, F (1, 116) = 33.63, $p < 0.001$, $\eta_p^2 = 0.23$, with the test group having a significantly higher rate of correctness ($M = 0.58$ $SD = 0.32$) than the restudy group ($M = 0.31$, $SD = 0.30$), t (118) = 4.80, $p < 0.001$, $d = 0.87$, 95%CI [0.16, 0.38]. There was no interaction between the two factors, F (1, 116) = 0.39, $p = 0.53$, $\eta_p^2 = 0.003$.

The FET was examined separately for the patients with schizophrenia and the healthy controls. For the healthy controls, the results showed a significantly higher recall rate in the test ($M = 0.77$, $SD = 0.26$) than in the restudy group ($M = 0.47$, $SD = 0.32$), t (58) = 4.02, $p < 0.001$, $d = 1.03$, 95%CI [0.15, 0.45]). Similarly, patients with schizophrenia recall rate was also significantly higher in the test ($M = 0.39$, $SD = 0.26$) than in the restudy group ($M = 0.15$, $SD = 0.16$), t (58) = 4.32, $p < 0.001$, $d = 1.11$, 95%CI [0.13, 0.35]).

As shown in Fig. 5 c, with the interference rate dependent variable, a 2 (Group: healthy controls vs. patients with schizophrenia) × 2 (Learning condition: test vs. restudy) ANOVA demonstrated that main effect of group was significant, F (1, 116) = 18.90, $p < 0.001$, $\eta_p^2 = 0.14$. The interference rate of the healthy controls ($M = 0.18$, $SD = 0.19$) was significantly lower than that of the patients with schizophrenia ($M = 0.31$, $SD = 0.21$). t (118) = 3.78, $p < 0.001$, $d = 0.65$, 95%CI [0.07, 0.21]. The main effect of learning condition was also significant, F (1, 116) = 39.62, $p < 0.001$, $\eta_p^2 = 0.26$. Whereby the interference rate in the test ($M = 0.14$, $SD = 0.15$) was significantly lower than that in the restudy group ($M = 0.35$, $SD = 0.22$), t (118) = 5.87, $p < 0.001$, $d = 1.12$, 95%CI [0.13, 0.27]. The interaction between the two factors was not significant, F (1, 124) = 0.71, $p = 0.40$, $\eta_p^2 = 0.006$.

Further, PI was tested separately for patients with schizophrenia and healthy controls. Results showed that for the healthy controls, the interference rate in the test condition ($M = 0.09$, $SD = 0.13$) was significantly lower than that in the restudy condition ($M = 0.26$, $SD = 0.21$), t (58) = 3.96, $p < 0.001$, $d = 0.97$, 95%CI [0.09, 0.26]). For patients with schizophrenia, the test ($M = 0.20$, $SD = 0.16$) was significantly lower than the restudy condition ($M = 0.43$, $SD = 0.20$), t (58) = 4.93, $p < 0.001$, $d = 1.27$, 95%CI [0.14, 0.32].

3.2.3. Mediation analyses

For the healthy controls (Fig. 6a). the results indicated that the indirect effect of the mediation test did not include 0 (*Effect* = 0.224, *SE* = 0.047, 95%CI [0.126, 0.315]), accounting for 74.8% of the total effect. Additionally, after controlling for the mediating variable, the proactive interference (PI), the direct effect of the independent variable (learning condition) on the dependent variable (R4 correct recall) is not statistically significant, with the confidence interval including 0 (*Effect* = 0.076, *SE* = 0.055, 95%CI [−0.035, 0.187]).

For the patients with schizophrenia group (Fig. 6b), the results indicated that the indirect effect of the mediation test did not include 0 (*Effect* = 0.122, *SE* = 0.047, 95%CI [0.050, 0.232]), accounting for 50.31% of the total effect. Moreover, after controlling for the mediating variable PI, the direct effect of the independent variable learning condition on R4 correct recall was not significant, with the interval including 0 (*Effect* = 0.120, *SE* = 0.060, 95%CI [−0.001, 0.241]). Additionally, we examined executive function and attention as mediating variables, PANSS and IQ measures as covariates for the patients with schizophrenia group, and found that they were not significant (See SM for details).

Consistent with Experiment 1, we further explored the role of the group as a moderating variable in the mediation. Bootstrap analysis results indicated no significant moderating effect of the group in the

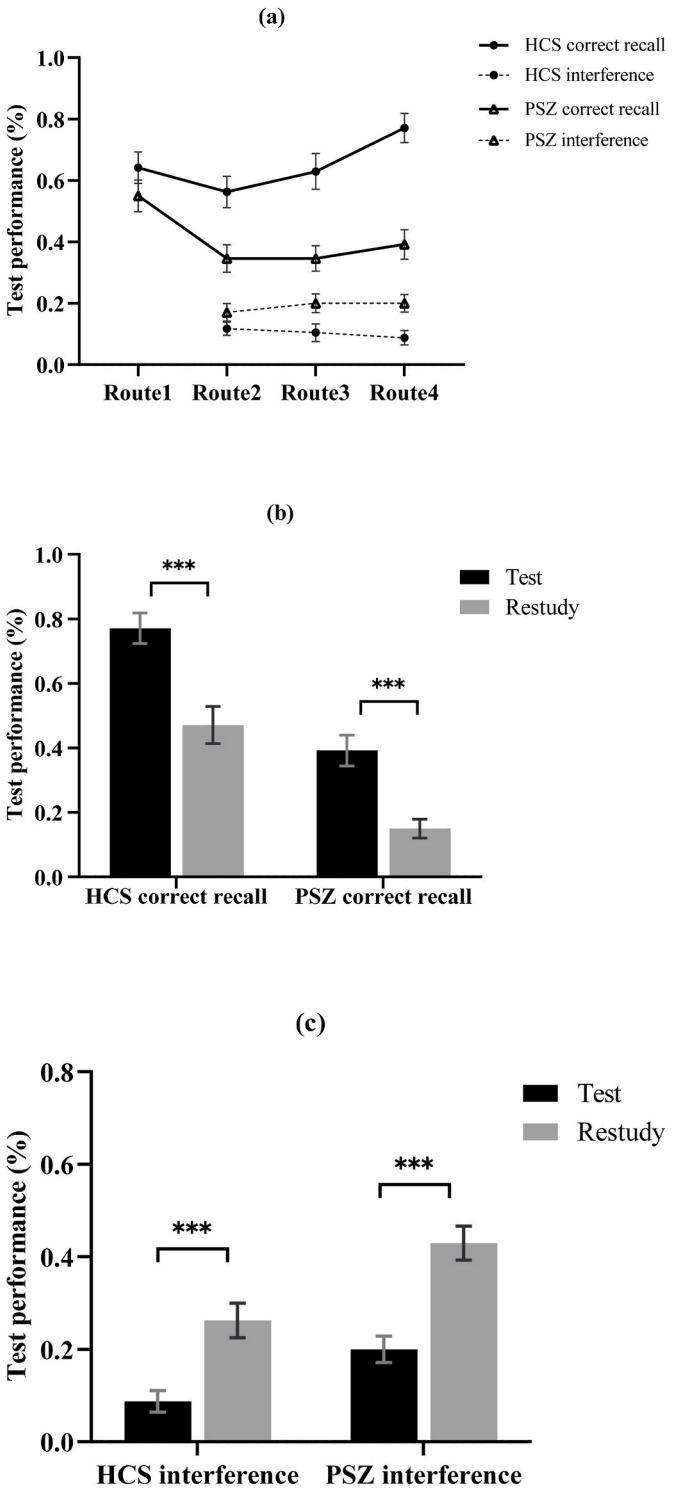

Fig. 5. (a) Correct recall and interference rate in Routes 1–4 for healthy controls (HCS) and patients with schizophrenia (PSZ). **(b)** Correct recall of healthy controls and patients with schizophrenia in Route 4. **(c)** Interference rates in healthy controls and patients with schizophrenia group in Route 4. ***$p < 0.001$; **$p < 0.01$; *$p < 0.05$.

learning condition on PI ($p = 0.535$), i.e., in both the patients with schizophrenia and the healthy controls, the learning condition increased correctness through reduced PI.

3.3. Discussion

Experiment 2 also validated the FTE in route learning within a 3D spatial background. Compared to 2D planar maps, the 3D spatial background involved dynamic video presentations, with buildings appearing sequentially. This format challenged participants' encoding and processing of the sequence in which buildings appeared, resulting in slightly lower accuracy compared to the 2D background. Nevertheless, with ongoing interim testing, the FET persisted in Route 4 for both patients with schizophrenia and healthy participants. The test group exhibited significantly higher accuracy in recalling Route 4 information compared to the restudy group, with significantly lower PI than the restudy group. This suggests that testing on Routes 1–3 significantly reduced PI in Route 4. Results from the mediation analyses indicated a significant mediating effect of PI reduction on the improvement in accuracy for both healthy participants and patients with schizophrenia.

4. General discussion

The current study, for the first time, investigated the FTE in spatial route learning using 2D planar maps and 3D spatial backgrounds as learning materials among patients with schizophrenia. The results revealed enhanced recall rates for both patients with schizophrenia and healthy control groups. Interim testing of previously learned materials reduced PI from prior learning and improved recall of subsequently learned information (Route 4). This aligns with previous research on healthy groups across various age populations (Aslan & Bäuml, 2016; Ma et al., 2022; Pastötter & Bäuml, 2019; Wang et al., 2020; Yang et al., 2020) and traumatic brain injury patients (Pastötter et al., 2013), suggesting that the FTE extends to individuals with inhibitory deficits, such as patients with schizophrenia. This advances the clinical application of the FTE in cognitively impaired populations.

Specifically, in the context of learning 2D planar maps (Experiment 1) and 3D spatial routes (Experiment 2), patients with schizophrenia exhibited lower immediate recall rates compared to the healthy control group under test conditions. Conversely, a reversed pattern was observed for proactive interference. This reflects that patients with schizophrenia generally demonstrate memory impairments and greater difficulty in inhibiting PI, as compared to healthy groups (Davidson & Heinrichs, 2003; Soriano et al., 2009). Nevertheless, the process of testing significantly improved memory retention for Route 4 among patients with schizophrenia in comparison to restudy, demonstrating a capacity of testing to inhibit PI similar to that observed in healthy controls. These findings address a research gap in exploring the existence of the FTE in spatial route learning within the context of cognitive impairment.

From the learning outcomes of 3D spatial Routes 1–4, under test conditions, the healthy group exhibited a consistent trend throughout the entire route learning process: an increase in interference rates corresponded to a decrease in accuracy across the four routes, and a decrease in interference rates correlated with an increase in accuracy between the test and restudy conditions. Patients with schizophrenia also showed performance improvements, with no significant decrease in PI but also no increase. Nevertheless, interim testing brought benefits, as the correct recall rate for Route 4 was significantly higher than that for restudy, and PI under test conditions was significantly lower than under restudy conditions. Many studies indicate a frequent association between FTE and a reduction in PI (Aslan & Bäuml, 2016; Bufe & Aslan, 2018; Yang et al., 2018). Specifically, these studies consistently observe that interim testing enhances the recall of new information while significantly reducing PI. A plausible inference is that the decrease in PI and the enhancement of new information recall represent a causal relationship, wherein interim testing reinforces new learning by shielding it from the detrimental effects of PI. Examination of the mediating effect in the learning outcomes of Route 4 revealed that interference rates played a complete mediating role between learning

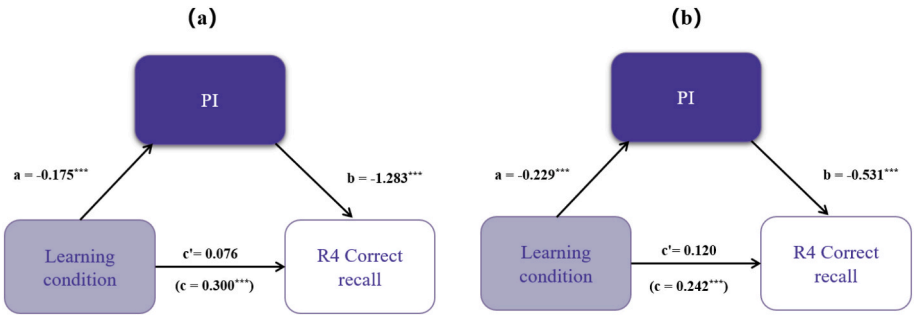

Fig. 6. Mediation model diagram between learning condition and correct recall of Route 4 (R4), where PI refers to proactive interference in Route 4. **(a)** Mediation model for the healthy control group. **(b)** Mediation model for patients with schizophrenia. ***$p < 0.001$; **$p < 0.01$; *$p < 0.05$.

conditions and correct recall, providing direct empirical evidence supporting the release from PI theory. This finding aligns with research on the FTE in spatial route information learning conducted with a sample of healthy university students (Ma et al., 2022).

Individuals exhibited slightly different learning outcomes between 2D and 3D routes. The healthy group's test scores for recall on Routes 1–4 remained relatively consistent. Patients with schizophrenia showed a slight increase in recall rates across Routes 1–4, but interference rates also increased. This could be attributed to the planar nature of 2D maps, allowing participants to see all buildings along the entire route during learning. Due to the high similarity among the four routes, confusion was more likely, leading to an increase in PI with continuous learning. Nevertheless, even in comparison to restudy, both the healthy group and patients with schizophrenia group exhibited better recall rates and lower PI on Route 4 under test conditions, demonstrating a FTE. This suggests that the "benefits" of interim testing may extend beyond interference reduction, promoting learning through alternative pathways. Examination of the mediating effect on the learning outcomes of Route 4 revealed that PI played a partial mediating role between learning conditions and correct recall, suggesting that in 2D map learning, interim testing might bring benefits through avenues other than just interference suppression. The Learning Engagement theory to some extent explains this result, indicating that interim testing contributes to the rebound of learning engagement during the iterative learning process, facilitating the acquisition of new information (Pastötter et al., 2011). Additionally, a comparison of overall learning outcomes between 2D and 3D revealed higher test scores in 2D. In 3D spatial background, buildings are presented sequentially, demanding more encoding and processing of the order of appearance, and requiring higher levels of cognitive resources. Buildings presented in a 2D background simplify the encoding and extraction of target information, eliminating "unnecessary" interference stimuli such as greenery, residential buildings, and the colors of landmark buildings. Although cognitive resource demands are lower, it is more prone to confusion. With continuous interim testing, participants' confidence and motivation in learning may be enhanced, thus improving route memory.

Combining the results across the two experiments, this study suggests that the observed FTE in patients with schizophrenia during spatial route learning is directly related to the reduction of PI induced by interim testing. However, there may be additional mechanisms at play. This indicates that the "benefits" of interim testing may extend beyond interference reduction. A comprehensive understanding of the underlying mechanisms of the FTE requires considering the participants' memory characteristics and the nature of the experimental materials. Additionally, this study aimed to investigate spatial route learning abilities in patients with schizophrenia. Although interim testing did not completely suppress the PI of previous content on new information for patients with schizophrenia, it significantly enhanced their learning and memory of new information. This paradigm effectively compensates for the susceptibility of patients with schizophrenia to irrelevant interference due to inhibition deficits, serving as a powerful means to improve their learning and memory. It holds significant application value in the cognitive rehabilitation training of patients with schizophrenia. Moreover, this effect may benefit other populations with memory difficulties, such as the elderly and individuals with cognitive disorders, potentially having broad applicability across diverse populations.

In conclusion, the present study provides new findings on testing to enhance learning of spatial route information in patients with schizophrenia. It offers direct empirical evidence for the release from PI theory and suggests that the benefits of testing are not confined to interference reduction alone. The impact of learning materials on cognitive resources influences the mechanisms through which testing facilitates subsequent learning of new information. Unfortunately, this study did not directly measure the cognitive load imposed by the learning materials. Future research could delve into the interaction between cognitive load and participants' memory characteristics as a starting point to further explore the mechanisms of the FTE.

CRediT authorship contribution statement

Yaoyao Tan: Writing – original draft, Methodology, Investigation, Data curation, Conceptualization. **Tiantian Li:** Writing – review & editing, Writing – original draft, Software, Formal analysis, Conceptualization, Data curation, Funding acquisition, Methodology. **Chunliang Yang:** Writing – review & editing. **Xiaoning Huo:** Resources, Funding acquisition. **Minghui Liu:** Visualization, Investigation. **Jing Zhang:** Visualization, Investigation. **Xiaofeng Ma:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Funding acquisition, Conceptualization.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jenvp.2024.102305.

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