General

Treatment of cognitive deficits in schizophrenia using a new technique of Cognitive Training in Virtual Reality: a pilot study

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Background

Cognitive impairments, prevalent in 75-80% of schizophrenia patients, severely impact rehabilitation and quality of life. Current therapies, including antipsychotics, have limited success in addressing these deficits. Virtual reality (VR) offers a promising avenue for cognitive training by providing realistic, interactive scenarios for skill application.

Objective

This study evaluates the efficacy of a novel VR-based cognitive training intervention in improving cognitive deficits in schizophrenia compared to standard treatment as usual (TAU).

Methods

A randomized clinical trial was conducted with 16 inpatients diagnosed with schizophrenia. Participants were allocated to either a VR intervention group, receiving six weekly sessions of VR cognitive training, or a control group undergoing TAU. Pre- and post-intervention assessments included the Trail Making Test, Positive and Negative Syndrome Scale, Frontal Assessment Battery, and Tower of London test. Two VR scenarios, "Supermarket" and "Beach," were developed to target working memory, attention, and executive functioning. Data were analyzed using t-tests and linear mixed-effects models.

Results

The VR intervention group showed significant improvements in frontal lobe functioning as measured by the Frontal Assessment Battery (FAB) and trends toward better executive function and attention. Scenario-specific analyses revealed reduced errors, omissions, and execution times across sessions. However, broader cognitive and psychiatric symptom improvements were limited and did not persist after multiple-comparison corrections.

Conclusion

VR cognitive training shows potential as an innovative tool for enhancing executive functioning in schizophrenia patients. While immediate task performance improved, broader cognitive impacts and psychiatric symptom reductions were minimal. Future research should focus on long-term efficacy, functional outcomes, and scalability of VR interventions.

1. INTRODUCTION

Cognitive impairment affects 75-80% of schizophrenia patients, significantly impacting rehabilitation, functioning, and quality of life.[1] These impairments pose a therapeutic challenge, as current antipsychotics have limited efficacy, especially on negative symptoms, despite some improvements with second-generation antipsychotics.[2-4]

Virtual reality (VR) shows promise as a versatile therapy for schizophrenia, addressing delusions, hallucinations, cognitive, and social skills.[5] This novel intervention enhances cognitive performance like cognitive remediation and allows users to apply these improved capabilities in a simulated, real-life context.[6]

Cognitive remediation, metacognitive training, social skills training, psychoeducation, family interventions are evidence-based treatments for cognitive stimulation,[7] but virtual reality is highly appealing, especially to young people, and enables realistic experiences with minimal ecological impact. We aimed to test a new VR-based therapy for cognitive symptoms, hypothesizing it would improve patients' cognitive domains more effectively than treatment as usual (TAU).

2. MATERIALS AND METHODS

2.1. PARTICIPANTS

Sixteen inpatients diagnosed with schizophrenia were recruited from May to October 2024 at the University Psychiatry Clinic "G. Rodolico" in Catania and the "Villa Chiara" Therapeutic Community in Mascalucia, Italy. Patients were selected through convenience sampling and randomly assigned using a computer-generated random number table to one of two groups: the VR intervention group or the control group. The VR intervention group participated in sessions designed to address attentional, mnemonic, and executive deficits, while the control group received treatment as usual (TAU), consisting of pharmacotherapy, psychoeducation, social skills training, and cognitive-behavioral therapy. Inclusion criteria required participants to have a DSM-5 diagnosis of schizophrenia, be clinically stable for at least three months, have no neurological or motor impairments affecting VR use, and be 18 years or older. Exclusion criteria included substance use disorders or an inability to provide informed consent.

2.2. OBJECTIVES

This study aims to evaluate the efficacy of a novel VR-based cognitive training intervention in improving cognitive deficits in schizophrenia patients. Specifically, the intervention targets working memory, attention, and executive functioning, and is compared to standard treatment as usual (TAU).

2.3. ASSESSMENT PROCEDURE

Both groups were assessed pre- and post-treatment with: Trial Making Test variants A, B, and B-A (TMT-A, TMT-B, TMT B-A),[8] Positive and Negative Syndrome Scale (PANSS),[9] Frontal Assessment Battery (FAB),[10] and Tower of London test (ToL),[11] to assess attention, executive skills, cognition, and psychotic symptoms.

2.4. INTERVENTION PROCEDURE

Intervention group received six VR-cognitive training sessions over 6 weeks, with one session weekly lasting about one hour, based on previous similar studies.[12] Each session involved two 3D interactive scenarios in non-immersive virtual reality, where patients executed specific tasks. Instructions were given beforehand, and the rater (EB) did not interfere to avoid influencing results. A facilitator from the therapeutic community staff supported the patients with prompts and feedback as needed, in line with current evidence.[13]

2.5. VIRTUAL REALITY SCENARIOS

The intervention utilized a computer screen and controller to engage patients with the virtual environment, using NeuroVR v.2.0 software to create two interactive 3D scenarios:

Scenario 1 - "Supermarket" (fig 1): Aims to improve working memory, attention, and executive skills. Similarly to the store scenario designed by Keefe et al.[14] for VRFCAT, it simulates grocery shopping. It includes three tasks of increasing difficulty, each with memory and execution subtasks. The patient memorizes five objects, navigates a virtual supermarket to collect these items, and brings them to the cash desk. The number of items is based on normative data from the Rey Auditory Verbal Learning Test (RAVLT) for schizophrenia patients.[15] Each task ends when all required items are correctly collected and placed on the cash desk. Participants can retry tasks without limits until advancing. Each new level requires memorizing and collecting more items (two additional in the second and last tasks). Errors, omissions, and any help needed are recorded.

Scenario 2 - "Beach" (fig 2): Aims to improve working memory, attention, and executive skills, particularly the latter two. In the scenario replicating a large open space with a beach and a bathing establishment, patients undertake three tasks, identifying objects in the environment by their proximity, shape, or color to foster focused and sustained attention. They must recall the initial instructions from the experimenter e.g. "Collect only the object X that are in contiguity with the object Y", utilizing their working memory, and navigate the tasks strategically in this complex setting to demonstrate their executive skills. The number of exercises per session is flexible, allowing the patient to repeat tasks as needed to complete the session. The execution time, number of errors, aids used, and omissions are all tracked.

The selection of these scenarios was guided by a preliminary focus group with patients, discussing common daily activities to decide on the most engaging and useful scenarios.

2.6. STATISTICAL ANALYSIS

To test our hypotheses, we used a comprehensive statistical approach. Our primary hypothesis was that the VR intervention group would show greater cognitive improvements than the TAU-only group. We evaluated normal distribution with the Shapiro-Wilk test and expressed continuous variables as mean ± standard deviation (SD) or median and interquartile range. Exploratory t-tests examined within-group changes and between-group differences, including paired t-tests for within-group comparisons and Welch's t-tests for between-group comparisons. We fitted a linear

Figure 1. Supermarket

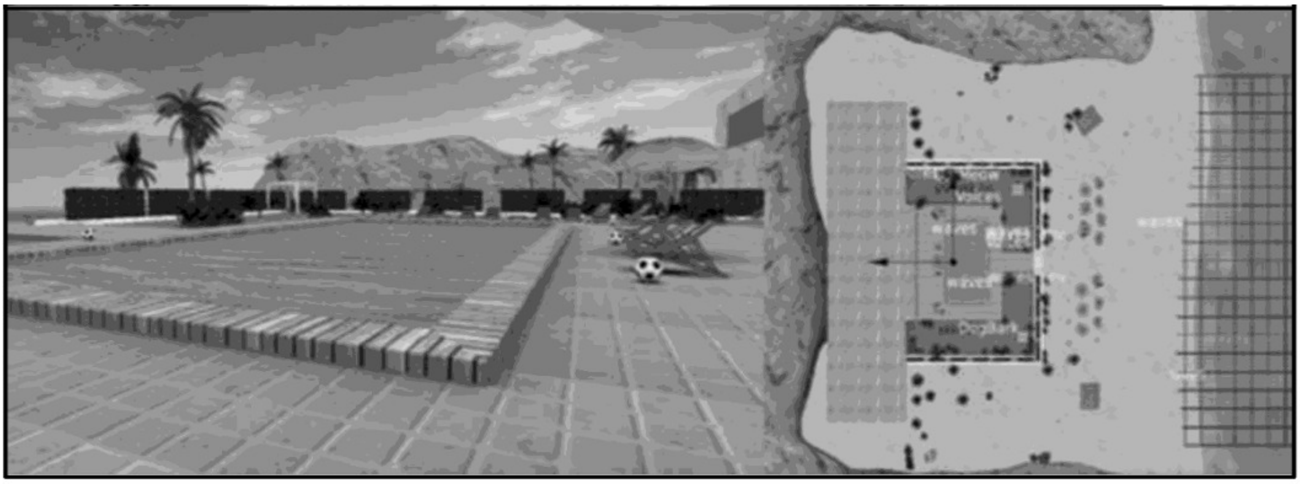

Figure 2. Beach

mixed-effects model: Outcome ~ Arm * Timepoint + (1|Participant), using F-tests to assess the significance of Arm, Timepoint, and their interaction. A p-adjusted value < 0.05 was considered statistically significant after FDR correction. Additional analyses for the intervention group included errors, omissions, aids, and execution time for tasks. Data were cumulated by session and analyzed descriptively. All analyses were performed using R version 4.1.0 with the lme4, lmerTest, and stats packages.

3. RESULTS

3.1. CHARACTERISTICS OF THE SAMPLE

All participants were Caucasian, long-term facility patients, recruited either at the facility or during quarterly clinic visits. One individual in the intervention group had a comorbid social anxiety disorder. All participants remained clinically stable and continued their established psychopharmacological treatments. All patients' demographic data are reported in Table 1.

Table 1. Characteristics of samples

	Intervention group (N=8)	Control group (N=8)
M/F	5/3	5/3
Mean age, males (SD)	37 years (7,21)	37 years (9,03)
Mean age, female (SD)	36 years (6,56)	33 years (7,21)
Duration of illness	15 years (4,53)	14 years (3,87)
Race - Caucasian	8	8
Educational levels		
middle school diploma	5	4
high school diploma	2	4
degree	1	0

Table 2. Average results from scenario 1 and 2 by VR-session. (Note: execution time is expressed in second (s); SD: standard deviation)

	Session	1	2	3	4	5	6
Scenario 1	Execution time	1220,125	1367,750	747,625	586,625	532,500	383,000
	SD	951,122	1075,765	558,168	521,293	410,190	279,691
	Error	1,500	1,500	0,875	0,500	0,375	0,000
	SD	2,138	1,773	1,246	0,756	0,744	0,000
	Omissions	2,250	2,750	1,375	0,875	0,500	0,375
	SD	1,389	1,753	1,598	1,126	0,756	0,518
	Aids	4,250	2,750	1,625	1,500	0,625	0,250
	SD	3,327	1,982	1,506	1,927	0,744	0,463
Scenario 2	Execution time	1602,375	1654,000	1399,500	1086,000	1099,250	817,250
	SD	1227,557	1172,538	1159,183	836,048	960,044	613,036
	Error	1,625	0,875	0,750	0,125	0,375	0,125
	SD	1,408	1,126	2,121	0,354	1,061	0,354
	Omissions	0,250	0,125	0,375	0,000	0,000	0,000
	SD	0,707	0,354	0,518	0,000	0,000	0,000
	Aids	3,875	2,250	2,500	0,750	0,500	0,375
	SD	5,276	2,435	4,567	1,165	1,069	0,744

3.2. TRAINING RESULTS SCENARIO 1 (SUPERMARKET)

The training session for scenario 1 (supermarket) in Table 3 shows a marked decrease in average execution time for the three tasks as sessions progressed, with reductions in errors, forgetfulness, and the need for aids indicating improvements in task completion and executive skills.

3.3 TRAINING RESULT SCENARIO 2 (BEACH)

For scenario 2 (beach), average completion times and errors also decreased over VR cognitive training sessions, as shown in Table 2. Execution times improved, the need for aids dropped, and errors nearly vanished after the third session. Omissions remained minimal, with a slight peak in the third session due to the simpler memory requirement of tracking object counts.

3.4. ASSESSMENT RESULTS

Assessment tests were administered at baseline and study end, with data summarized in Table 3. The VR cognitive training showed some improvements in executive skills and attention, although fewer effects remained significant after correction. The TMT-B revealed a significant main effect of Timepoint (F = 10.824, p-adjusted = 0.0486), suggesting improvement over time in both groups. FAB demonstrated the most robust effects, with a significant main effect of Arm (F = 11.1622, p-adjusted = 0.0486) and a highly significant interaction effect (F = 30.5569, p-adjusted = 0.0027), providing strong evidence of greater improvement in the intervention group for frontal lobe functioning. This was further supported by a significant between-group difference at the post-intervention timepoint (T1) in the t-test results (t = -5.6392, p-adjusted = 0.0050). Interestingly, after correction, the ToL test and TMT B-A scores no longer showed statistically significant effects, although trends towards improvement were observed. The PANSS subscales showed no significant effect.

4. DISCUSSION

This study demonstrates the potential of VR in treating schizophrenia spectrum disorders, consistent with similar studies.[16,17] After correction, VR cognitive training plus TAU significantly improved cognitive functions compared to TAU alone.

FAB scores showed significant improvements in frontal lobe functioning for the intervention group, and TMT-B scores indicated enhanced executive function and attention in both groups. Other cognitive measures like the ToL test and TMT A and B-A showed improvements but were not statistically significant. PANSS subscales showed no significant changes, meaning cognitive improvements did not reduce psychiatric symptoms. VR scenarios showed reduced execution times, errors, and need for assistance, particularly in simpler tasks. These findings suggest that VR cognitive training benefits frontal lobe functioning and executive function in schizophrenia. Future research should examine long-term effects, functional outcomes, quality of life, and broader cognitive and psychiatric impacts. Limitations include a small sample size, focus on specific cognitive domains, lack of long-term follow-up, and the absence of trial registration, which was not conducted due to the feasibility nature of the study.

Table 3. Analysis of Cognitive and Psychiatric Measures: T-test Results and Linear Mixed-Effects Models

Scale	Control T0	T-test Results (t, p-adjusted)	Linear Mixed-Effects Model (F, p-adjusted)
ToL – C – T0	10.51 (5.63)	Between-group T0: t = 0.2202, p = 0.8905	Arm: F = 0.0165, p = 0.9216
ToL – C – T1	11.68 (5.63)	Between-group T1: t = 0.0184, p = 0.9856	Timepoint: F = 1.5937, p = 0.7108
ToL – I – T0	9.84 (6.42)	Intervention T0 vs T1: t = -3.4213, p = 0.1000	Arm:Timepoint: F = 0.0677, p = 0.9054
ToL – I – T1	11.62 (6.58)	Control T0 vs T1: t = -0.5140, p = 0.8259	
TMT-A – C – T0	65.88 (28.51)	Between-group T0: t = -0.2051, p = 0.8905	Arm: F = 0.0100, p = 0.9216
TMT-A – C – T1	62.12 (9.54)	Between-group T1: t = 0.0295, p = 0.9856	Timepoint: F = 1.2630, p = 0.7108
TMT-A – I – T0	69.88 (47.21)	Intervention T0 vs T1: t = 1.4218, p = 0.5485	Arm:Timepoint: F = 0.1776, p = 0.9054
TMT-A – I – T1	61.62 (46.94)	Control T0 vs T1: t = 0.4184, p = 0.8259	
TMT-B – C – T0	153.00 (94.82)	Between-group T0: t = -0.8978, p = 0.6356	Arm: F = 1.2102, p = 0.7108
TMT-B – C – T1	89.00 (11.54)	Between-group T1: t = -1.2652, p = 0.5807	**Timepoint: F = 10.8240, p = 0.0486***
TMT-B – I – T0	217.00 (177.94)	Intervention T0 vs T1: t = 3.1980, p = 0.1088	Arm:Timepoint: F = 0.0638, p = 0.9054
TMT-B – I – T1	162.12 (163.06)	Control T0 vs T1: t = 2.0127, p = 0.4191	
TMT B-A – C – T0	87.12 (75.47)	Between-group T0: t = -0.8767, p = 0.6356	Arm: F = 1.7228, p = 0.7108
TMT B-A – C – T1	26.50 (8.42)	Between-group T1: t = -1.7507, p = 0.4922	Timepoint: F = 8.7189, p = 0.0709
TMT B-A – I – T0	136.38 (139.83)	Intervention T0 vs T1: t = 1.9430, p = 0.4191	Arm:Timepoint: F = 0.5735, p = 0.8745
TMT B-A – I – T1	100.50 (119.26)	Control T0 vs T1: t = 2.2482, p = 0.3561	
FAB – C – T0	12.00 (2.20)	Between-group T0: t = -1.5275, p = 0.5428	**Arm: F = 11.1622, p = 0.0486***
FAB – C – T1	10.12 (1.36)	**Between-group T1: t = -5.6392, p = 0.0050***	Timepoint: F = 0.3772, p = 0.8745
FAB – I – T0	14.00 (2.98)	Intervention T0 vs T1: t = -3.5496, p = 0.1000	**Arm:Timepoint: F = 30.5569, p = 0.0027***
FAB – I – T1	15.50 (2.33)	Control T0 vs T1: t = 4.2548, p = 0.0679	
PANSS-P – C – T0	18.12 (7.41)	Between-group T0: t = 0.8255, p = 0.6356	Arm: F = 1.4227, p = 0.7108
PANSS-P – C – T1	19.62 (8.30)	Between-group T1: t = 1.3516, p = 0.5485	Timepoint: F = 0.0634, p = 0.9054
PANSS-P – I – T0	14.62 (9.43)	Intervention T0 vs T1: t = 1.2556, p = 0.5807	Arm:Timepoint: F = 0.3741, p = 0.8745
PANSS-P – I – T1	14.00 (8.35)	Control T0 vs T1: t = -0.4363, p = 0.8259	
PANSS-N – C – T0	20.75 (10.10)	Between-group T0: t = 0.2530, p = 0.8905	Arm: F = 0.2785, p = 0.9054
PANSS-N – C – T1	22.25 (10.54)	Between-group T1: t = 0.6478, p = 0.7307	Timepoint: F = 0.0378, p = 0.9166
PANSS-N – I – T0	19.50 (9.67)	Intervention T0 vs T1: t = 1.0000, p = 0.6311	Arm:Timepoint: F = 0.1511, p = 0.9054
PANSS-N – I – T1	19.00 (9.50)	Control T0 vs T1: t = -0.2930, p = 0.8905	
PANSS-G – C – T0	44.38 (17.34)	Between-group T0: t = 0.6633, p = 0.7307	Arm: F = 1.2285, p = 0.7108

Scale	Control T0	T-test Results (t, p-adjusted)	Linear Mixed-Effects Model (F, p-adjusted)
PANSS-G – C – T1	50.25 (17.00)	Between-group T1: t = 1.4442, p = 0.5485	Timepoint: F = 0.8234, p = 0.7882
PANSS-G – I – T0	38.50 (18.08)	Intervention T0 vs T1: t = 1.2104, p = 0.5807	Arm:Timepoint: F = 1.3759, p = 0.7108
PANSS-G – I – T1	37.75 (17.61)	Control T0 vs T1: t = -1.0465, p = 0.6255	
PANSS-T – C – T0	83.25 (21.31)	Between-group T0: t = 0.8550, p = 0.6356	Arm: F = 1.0818, p = 0.7108
PANSS-T – C – t1	87.62 (34.75)	Between-group T1: t = 1.0999, p = 0.5807	Timepoint: F = 0.0681, p = 0.9054
PANSS-T – I – T0	71.75 (31.51)	Intervention T0 vs T1: t = 1.1657, p = 0.5807	Arm:Timepoint: F = 0.4255, p = 0.8745
PANSS-T – I – T1	69.88 (29.59)	Control T0 vs T1: t = -0.4632, p = 0.8259	

ToL: Tower of London test; TMT A: Trail Making Test Part A; TMT B: Trail Making Test Part B; TMT B A: Difference between Trail Making Test Part B and A; FAB: Frontal Assessment Battery; PANSS P: Positive and Negative Syndrome Scale - Positive symptoms; PANSS N: Positive and Negative Syndrome Scale - Negative symptoms; PANSS G: Positive and Negative Syndrome Scale - General psychopathology; PANSS T: Positive and Negative Syndrome Scale - Total score. T0: Baseline; T1: Post-intervention; * Statistically significant ($p < 0.05$) after Benjamini-Hochberg correction for multiple comparisons.

5. CONCLUSIONS

This study suggests that VR cognitive training may benefit individuals with schizophrenia, particularly in enhancing executive functioning. While task performance improved, effects on most cognitive measures and psychiatric symptoms were limited. The intervention's potential lies in its scalability and adaptability. Further research is needed to fully understand its efficacy and potential for improving functional outcomes.

AUTHOR CONTRIBUTIONS

E.B. conceived and developed the original idea, supported by M.S.S.. E.B and A.F. administered the VR treatment, collected data and assessments, and wrote the original manuscript and P.C. collaborated in data collection and assessment, and with M.S.S., in the recruitment of subjects too. A.P. performed the statistical analysis. M.S.S., P.C. and A.F. revised the paper. M.S.S., P.C., E.A., A.F. G.A., R.A. supervised the project and provided organizational support and critical feedback. All Authors have read and approved the final version of the manuscript.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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