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Research paper

Ecological virtual reality-based cognitive remediation among inpatients with schizophrenia: A pilot study

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ABSTRACT

Schizophrenia presents a considerable clinical challenge due to limited progress in promoting daily-life functioning among diagnosed individuals. Although cognitive remediation (CR) has emerged as a promising approach to improving cognitive and functional outcomes in schizophrenia, its effectiveness among inpatients and within hospital environments—where opportunities to practice skills in real-world contexts are limited—remains unclear. Here, we aimed to establish the feasibility and initial efficacy of a short, ecological virtual reality-based CR training (CR-EVR) in acute mental health inpatient settings. Efficacy was assessed at four levels: training engagement, near transfer, far transfer, and ecological transfer. Twenty-three inpatients with schizophrenia (Male: 33.3 ± 8.5; 4 Female) completed 8, 20-min CR-EVR sessions, with exercises training the cognitive abilities of inhibition, planning, working memory, shifting, self-initiation, persistence, and attention. Their cognitive functioning, schizophrenia symptoms, functional capacity, and participation in occupations were evaluated pre- and post-training to address four levels of effectiveness. Of the recruited participants, 25.8 % dropped out. Inpatients who completed the full protocol reported high rates of satisfaction (1-not satisfied; 5-very satisfied)) from the intervention (Median = 4, IQR:3.5–5). Post-training, significant improvements were found in the trained cognitive components (intervention engagement: $-6.58 < t/Z < 2.02$, $p < .05$), general cognitive functioning ($-2.59 < t/Z < 2.29$, $p < .05$), functional capacity ($t = -2.9$, $p < .05$), and diversity of participation in everyday activities ($t = -3.36$, $p < .05$). This preliminary study suggests that CR-EVR may be a feasible and practical tool to enhance cognitive and ecological outcomes in short-stay acute inpatient settings. Subject to further research, such intervention may be considered an add-on to current practices that promote recovery and health among inpatient populations.

1. Introduction

Schizophrenia is a major health challenge, imposing a substantial burden on individuals and society in general (Vos et al., 2017; Boland and Verduin, 2021). This burden largely stems from significant limitations in participation in daily activities across major life areas including self-care, employment, leisure, and domestic responsibilities. These difficulties have been robustly demonstrated through objective parameters (such as number of performed activities and occupations, and frequency of the participation—intensity) (Granholm et al., 2020; Green et al., 2015; Harvey et al., 2019) and initially reported in subjective dimensions of enjoyment and satisfaction (Lipskaya-Velikovsky et al., 2016). In addition, there is robust evidence of limitations in functional capacity—the ability to perform everyday activities in a controlled environment, versus actual engagement in occupations in real-life environments (Bowie et al., 2008; Harvey et al., 2019). Altered functional capacity, which is primarily assessed through the simulation of predefined everyday tasks, further interrupts the possibility of participation (Bowie et al., 2008; Harvey et al., 2019). To date, despite a variety of available anti-psychotic medications and psycho-social interventions, improvement in daily life participation over time in schizophrenia remains limited, leading to prolonged debilitation (Boland and Verduin, 2021; Harvey et al., 2019).

Participation, being defined as engagement in daily-life situations

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through the performance of activities and occupations in a scope of life areas in one's natural environment (the World Health Organization, 2001), represents an ecological perspective. Participation is considered an important outcome of health-promoting interventions (World Health Organization, 2001). In the mental health literature, the term "everyday functioning" is often used to address selected aspects of objective dimensions of participation (e.g., the number of activities, level of independence, or the quality of performance) within specific daily life areas, such as employment, house holding or medication management, rather than the comprehensive construct (Harvey et al., 2019; Mucci et al., 2021; McCutcheon et al., 2023). Participation in daily life activities relies on personal (cognitive and psychological functions), environmental (support and accessibility), and occupational (novelty and demands) factors (Krupa et al., 2016). Cognitive impairments are recognized as a core feature of schizophrenia (Sheffield et al., 2018; Harvey et al., 2019). The prevalence of cognitive impairments in this population has been reported by various studies to be 60–80 % (Harvey et al., 2022; Parlar and Heinrichs, 2021). There is evidence showing deficits in a range of cognitive domains in schizophrenia (e.g., working memory, attention/vigilance, learning, reasoning, problem-solving, speed of processing, and social cognition). Still, there is a consensus in the literature that cognitive functioning in schizophrenia is mostly characterized by general impairment rather than by a failure in a certain domain (Harvey et al., 2019; DeTore et al., 2019; Green et al., 2015). Cognitive impairments were suggested to significantly contribute to limitations in participation and were found to account for up to 34 % of its variance (Green et al., 2015).

Cognitive remediation (CR)—targeting one or more cognitive domains (e.g., attention, memory, executive function) using mechanisms of learning and plasticity through repeated training—has been recognized as a consensus intervention approach for improving cognitive impairments in schizophrenia, often yielding small-to-medium effectiveness (Bowie et al., 2020; DeTore et al., 2019; Fitapelli and Lindenmayer, 2022; Lejeune et al., 2021; Vita et al., 2021). Building on findings that cognitive enhancement serves as a mechanism for improving functional outcomes, an ultimate goal of CR is improving functional outcomes by addressing cognitive skills with a direct link to daily-life functioning and generalizing cognitive gains to daily-life activities (Bowie et al., 2020; DeTore et al., 2019; Fitapelli and Lindenmayer, 2022). Still, the ability to improve functioning in daily life using CR strategies is debated, since considerable variability was found across studies with a gap between cognitive and functional gains (Bowie et al., 2020; DeTore et al., 2019; Fitapelli and Lindenmayer, 2022; Kambeitz-Ilankovic et al., 2019; Lejeune et al., 2021; Vita et al., 2021). Interestingly, the effectiveness of CR was found to improve substantially when practicing cognitive skills and strategies in the context of everyday life environments and occupations (Bowie et al., 2020; Lejeune et al., 2021).

Notably, most research examining the effectiveness of CR in schizophrenia was conducted among outpatients (Fitapelli and Lindenmayer, 2022; Kambeitz-Ilankovic et al., 2019; Lejeune et al., 2021; Vita et al., 2023), limiting the conclusions regarding its implementation in inpatient settings. The inpatient setting, serving a significant number of individuals with schizophrenia, poses a unique challenge for fostering cognitive training and transfer of learned skills to daily life participation due to its restrictive nature and the vulnerable health status of the inpatients. Studies on the effectiveness of CR in inpatient settings involved either long-term hospitalized individuals (e.g., Lindenmayer et al., 2008), very vulnerable populations such as forensic patients, or individuals with persistent symptoms, or experiencing challenges about community placement (e.g., Ahmed et al., 2015), applying mostly lengthy interventions with over 50 h of cognitive training (Ahmed et al., 2015; Cella et al., 2020). These studies showed notable improvements in cognitive performance but limited impact on vocational or overall everyday functioning (Cella et al., 2020). The only study employing a short (<4 h) computerized CR with acute inpatients demonstrated good feasibility and acceptability (Tsapekos et al., 2019). However, although training led to cognitive improvement, it had a limited impact on the ecological outcome of daily life functioning (Tsapekos et al., 2019).

Commonly, cognitive training is computerized (Harvey et al., 2018), while virtual reality (VR) is of potential benefit offering opportunities for simulation of ecological environments and tasks (Jahn et al., 2021; Perra et al., 2023). By providing multisensory experiences, interactive feedback, and playful design, ecological virtual reality (EVR) creates a sense of presence akin to real-life experiences (Perra et al., 2023), and stimulates genuine cognitive, emotional, and behavioral responses. In this way EVR has the potential to enhance the transfer of acquired skills to daily life (Jahn et al., 2021; Perra et al., 2023). In schizophrenia, VR was previously demonstrated to be feasible and effective for the improvement of general cognitive functioning and specific cognitive domains, mainly attention and executive function in outpatient populations (Jahn et al., 2021; La Paglia et al., 2016; Perra et al., 2023). Yet, most studies have not examined its effect on daily-life participation or failed to find changes in this type of outcome measure (Jahn et al., 2021; La Paglia et al., 2016; Perra et al., 2023). The few studies investigating the effectiveness of EVR (i.e., job interview training or virtual supermarket) reported a mixed trend of changes in the trained functional skills (Humm et al., 2014) or no change (Plechatá et al., 2021).

Here, we aimed to establish the feasibility and initial efficacy of a short CR intervention using an ecological, virtual reality-based training (CR-EVR) in acute mental health inpatient settings. More specifically, feasibility was assessed through drop-out rate and level of satisfaction with the intervention. Initial effectiveness was assessed across four levels based on the recommended approach for estimating the effectiveness of computerized CR (Harvey et al., 2018): (1) training engagement—improvement in metrics of the EVR training software; (2) near transfer—improvement in standardized cognitive tests following EVR training; (3) far transfer—improvement in functional capacity and symptom severity; and (4) ecological transfer—improvement in indices of the participation (Harvey et al., 2018). We hypothesized that CR-EVR would effectively address the limitations of inpatient environments for effective implementation of CR; it will be feasible and will contribute to the improvement at 4 levels: cognitive functioning, functional capacity, symptoms severity, and participation. No other study to date, to our knowledge, has examined CR-EVR intervention in an inpatient setting. Moreover, most studies addressed everyday functioning as an outcome, while participation is a more comprehensive measure in line with the WHO definition (World Health Organization, 2001).

2. Methods

2.1. Participants

The study included 31 participants, aged 18–58 years, all diagnosed with psychotic disorder (Table 1). The sample size calculation was based on a previous study on CR effectiveness for functional capacity improvement (Ahmed et al., 2015), the most proximal measure to the target outcomes of this study. Considering effect sizes ranging between Cohen's d of 0.59 and 0.65 found in the Ahmed et al. study and acknowledging possible differences between the outcomes (functional capacity versus everyday functioning), we opted to use a conservative estimate of Cohen's $d = 0.59$. With this effect size, a power of 0.85, and an alpha level of 0.05, the minimal required sample size was determined to be 23. Given a possible attrition rate of 30 % from the intervention, we recruited 31 individuals. Participants were recruited from the short-stay, acute wards of a regional mental health center in Israel. The inclusion criteria were a formal diagnosis of schizophrenia or schizoaffective disorder, age between 18 and 60 years, a minimum of two weeks of inpatient stay, and at least two weeks on a stable neuroleptic medication regimen. The following exclusion criteria were employed: comorbidity with neurological and/or neurodevelopmental health conditions; substance abuse in the past 6 months (based on both medical chart and self-report); hospital staying longer than 3 months; current

Table 1
Demographic characteristics (N = 31).

p	Difference between groups	Dropout (N = 8)	CR-EVR (N = 23)		
	tT-test	Mean (SD)	Mean (SD)		
		Range	Range		
0.45	0.76-	36.38 (12.97) 20–58	33.3 (8.53) 18–53		Age (years)
0.45	−-0.79	14.5 (13.31) 0–30	10.46 (9.15) 0–35		Illness duration
0.75	0.36	21.88 (8.2) 14–37	22.73 (4.74) 17–36		Age at onset
0.06	2.03	10.5 (7.56) 3–21	(5.8) 16.35 7–32		Current hospitalization (weeks)
p	Mann-Whitney Z	Median (IQR(Range	Median (IQR) Range		
0.45	0.76-	12 (8–14) 8–14	12 (12–14) 11–16		Years of education
0.72	0.36-	11)−– 3 (1 1–14	3 (1–6) 1–20		N. hospitalizations
0.95	1.67-	3.5 (2.75–6) 2–12	5 (4–8) 3–16		Hospitalization period before the study (weeks)
p	$^2\chi$	N (%)	N (%)		
0.24	1.37	5 (62.5 %)	19 (83 %)	Men	Gender
		3 (37.5 %)	4 (17 %)	Women	
0.028	10.8*	1 (12.5 %)	16 (69.6 %)	Yes	Native-born
		7 (87.5 %)	7 (30.4 %)	No	
0.67	0.8	7 (87.5 %)	19 (82.6 %)	Bachelor	Marital status
			2 (8.7 %)	Married	
		1 (12.5 %)	2 (8.7 %)	Divorcee	
0.35	4.5	5 (62.5)	18 (78.3 %)	Nuclear family	Living situation
		1 (12.5 %)	2 (8.7 %)	Alone	
		1 (12.5 %)	2 (8.7 %)	Spouse/children	
		1 (12.5 %)	1 (4 %)	Rehabilitation housing	
0.93	0.01	6 (75 %)	16 (69.6 %)	Schizophrenia	Main diagnosis
		2 (25 %)	7 (30.4 %)	Schizoaffective	
0.72	0.67	4 (50 %)	14 (60.9 %)	No	Work before hospitalization
		4 (50 %)	9 (39.1 %)	Yes	
0.03	4.5*	3 (62.5 %)	18 (78.3 %)	Yes	Previous experience with computer games
		5 (37.5 %)	5 (21.7 %)	No	
0.02	5.9*	0	11 (47.8 %)	Yes	Previous experience with VR technologies
		8 (100 %)	12 (52.2 %)	No	

Note:
* $p < .05$.

electroconvulsive therapy; and legal guardian. The participants were hospitalized in open conditions with weekend vocations and were given the option of leaving the hospital grounds in the afternoon upon individual request.

2.2. Design and procedures

This pilot study employed a quasi-experimental design with a pre-post format and utilized convenience sampling. The study was approved by the Institutional Review Board, and all participants provided written informed consent after receiving a detailed explanation of the study. Data collection lasted from October 2016 to December 2018.

Participants underwent baseline and post-intervention evaluations using standard tools, all within a single meeting lasting about 2 h. Tests were administered in a random order. After baseline, participants received 4 weeks of CR-EVR training alongside treatment as usual (TAU), which included pharmacological management, risk and acute-illness management, and basic life skills training. TAU did not include neurocognitive interventions. Baseline assessments were repeated post-intervention. Two professionals were involved in administering study procedures: one conducted pre- and post-training evaluations, while the other delivered the intervention sessions. Their roles remained consistent throughout the study to minimize bias.

2.3. Measurements and tools

2.3.1. Feasibility measure

Individuals' experience of satisfaction with the intervention was measured to estimate the feasibility of the intervention. The measure was designed for this study based on the Client Satisfaction Questionnaire (CSQ) (Attkisson and Greenfield, 1999) (items 1–5) and recommendations for the usage of VR for cognitive training (item 6) (Kizony, 2018). This measure addressed: (1) general satisfaction with CR training, (2) satisfaction with EVR as a cognitive training platform, (3) perceived cognitive functioning progress through the training, (4) perceived everyday functioning progress following the treatment, and (5) interest in participating in such an intervention in future routine care, (6) motivation levels within the CR-EVR. The last item (item #6) addresses the faculty of ecological virtual reality to be motivating being explicitly connected to daily life and due to user experience with advanced technologies. Each item was scored on a 5-point Likert scale, ranging from 1 (not satisfied/not interested) to 5 (very satisfied/very interested), and responses were collected upon intervention completion.

The evaluation for the efficacy was done with reliable and valid tools for schizophrenia and they were organized into 4 levels:

(1) Intervention engagement was quantified based on improvements in training tasks, measured using the cognitive training software's embedded evaluation modules. For a detailed description please see the intervention description and Shochat et al. (2017).

(2) Near transfer of training benefits to cognitive function was

assessed using the following standard, reliable and valid, non-computerized cognitive assessments:

The Neurobehavioral Cognitive Status Examination (COGNISTAT) (Mitrushina et al., 1994) was employed for the evaluation of a profile in five domains: language (naming, repetition, and language understanding), visuomotor organization, memory, calculation, and reasoning (abstract thinking and judgment) (test-retest reliability for the subscales: $r > 0.78$); The paper-and-pencil version of the Trail Making Test (TMT) (Gaudino et al., 1995) was used to evaluate processing speed, sequencing, mental flexibility, and visual–motor skills (test-retest reliability: TMT-A: $r = 0.79$, TMT—B: $r = 0.89$); The Category Fluency Test (CFT) (test-retest reliability: $r = 0.73$) (Spreen and Strauss, 1998) was used for evaluation of the verbal speed of processing.

(3) Far transfer of training benefits included assessments for schizophrenia symptom severity and functional capacity. Specifically, the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1988) was used to evaluate schizophrenia's positive and negative symptoms severity and general psychopathology. The Observed Tasks of Daily Living – Revised (OTDL-R) (Diehl et al., 2005) performance-based test wasre functional capach simulation of common daily life activities in three areas: taking medications, telephone use, and financial management. The total score is calculated to represent general functional capacity.

(4) Ecological transfer was assessed using the Adults Subjective Assessment of Participation (ASAP) (Jarus et al., 2006), which evaluates ecological, real-life participation based on the patient's self-report. This tool covers 52 activities across 7 life areas: domestic life, entertainment, and recreation, taking care of others, learning and applying knowledge, sport and physical activities, self-care, quiet leisure activities, and vocational and spiritual activities. The total scores encompass participation diversity (number of participated activities), intensity (frequency of participation), satisfaction with participation, and enjoyment. The ASAP addresses daily life activities that were available for participants either in the hospital (e.g., communication with family and friends by phone or messaging, outdoor jogging) or out of the hospital upon individual request (e.g., activities with children and family, bills' payment, making laundry of personal clothes or shopping for food for weekend and personal supplies that are not provided by the hospital. An example of a similar usage of the tool with an inpatient population may be seen (Lipskaya-Velikovsky et al., 2017).

2.4. Study intervention

The Functional Brain Trainer (FBT, Intendu Ltd.; Shochat et al., 2017), a VR platform, utilizes a motion-based camera (Kinect) to simulate real-life environments and daily tasks, such as running a food truck, managing a bus station, and working in a supermarket, for cognitive training. The FBT targets the cognitive domains of response inhibition, planning, working memory, working memory with manipulation, shifting, self-initiation & persistence, and sustained, selective, and divided attention through eight target games. Individual difficulty levels are dynamically adjusted in real-time to achieve a 60–80 % success rate. The FBT provides real-time feedback and a summary score after each game for users, with detailed training parameters of response time, success rate, and level of difficulty available to clinicians. In the FBT software, a user account is created for each individual. Specific games are pre-defined for training, along with session duration for each account. In addition, the software automatically saves the individual's training history for each game and session, including the level of difficulty and success rate, as part of an algorithm for the training personalization. In this study, the protocol was pre-defined for all participants as indicated below and operated by one research staff member.

The FBT software included an evaluation module that includes measurement of inhibition, persistence, working memory, shifting, and planning. The evaluation module tasks are designed similarly to those for the training, but the level of difficulty of the evaluation tasks is preset in the same way for all the participants with a graduate increase. The final score for each task is produced based on the success rate and response time.

The intervention protocol, tailored to the realities of an acute hospital stay, consisted of eight 20-min sessions, conducted 2–3 times per week. Each cognitive component was practiced through 2 to 5-min mini-games within a single session, accumulating a total of 20 min of practice for each component (Fig. 1). All participants completed a similar protocol, but training difficulty was adapted given individual performance. The training was accompanied by a skilled occupational therapist who was blind to the results of the evaluations, ensuring the technical aspects of the intervention and providing facilitation to support adherence to the 20-min protocol. The encouragement for training completion was provided only in case the participant expressed a desire to stop the training. It included short and general statements (e.g., "Well done, you can keep going, you have only two minutes before training is complete for today"). Upon completion of the full 8 sessions of the intervention, participants were asked to report their experience with the intervention using a feasibility and satisfaction questionnaire.

2.5. Data analysis

Data analysis was performed using SPSS, Version 28 (IBM Statistics). Descriptive statistics characterized the study sample. The assumption of normal distribution was tested using the Shapiro–Wilk test. To assess the feasibility of the intervention, we calculated the drop-out rate (%) and depicted satisfaction with the intervention using descriptive statistics (Median and IQR). To assess the effectiveness of the intervention across the 4 levels (intervention engagement, near, far, and ecological transfer) we analyzed the differences between baseline and post-intervention outcomes using paired *t*-tests or the Wilcoxon test, depending on the data distribution. The effect size was calculated using the r-value, as recommended for clinical studies (Brydges, 2019), with values of 0.1, 0.3, and 0.5 representing small, medium, and large effects, respectively. In addition, we calculated improvement rates as the difference between post-intervention- and baseline scores. Correlations between improvement rates and demographic variables were examined using the Spearman correlation coefficient for further understanding of potential intervening factors. Differences in improvement rates by gender and employment status were assessed with the Mann-Whitney test. A significance level of 0.05 was applied to all statistical tests.

3. Results

3.1. Study population

Table 1 provides socio-demographic data for participants who completed the intervention ($N = 23$), and those who dropped out ($N = 8$), and a comparative analysis between the two groups. On average, the participants were 33.3 years old (SD = 8.5) and 50 % of them had at least 12 years of education (IQR: 12–14). Nineteen (83 %) of the participants were men, 19 (83 %) of participants were single, and 18 (78.3 %) were living with their nuclear family before their hospitalization. Fourteen (60.9 %) participants were unemployed before hospitalization. The average age for the onset of schizophrenia symptoms was 22.7 ± 4.7 years, and patients underwent an average of 4.6 hospitalizations. 78 % of the participants have used or currently use a computer and 47.8 % had experience with a virtual reality system in the past.

3.2. Feasibility of the intervention

The intervention procedures were completed in full by 74.2 % (23 of 31; 25.8 % drop-out rate) of the participants who completed baseline assessments. Reasons for drop-out were: worsening of the psychiatric symptoms ($N = 3$), unexpected discharge (N = 3), and reluctance to continue the participation in the study ($N = 2$). Participants who

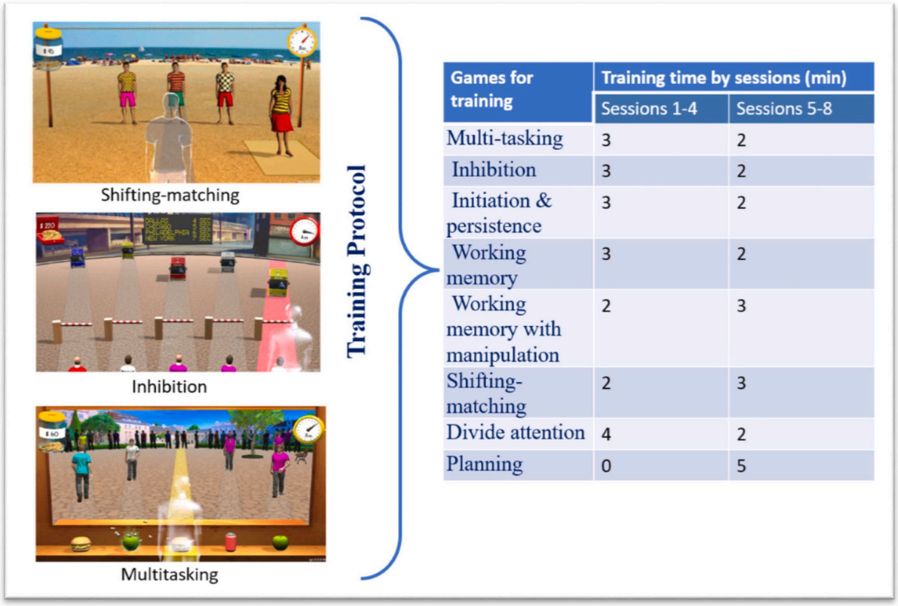

Fig. 1. Training protocol including cognitive tasks by sessions using the Functional Brain Trainer (FBT, Intendu, Ltd). (Note: The same protocol was applied to all participants.)

dropped out were more likely to be not native-born and to have no previous experience with computer games and/or VR technology compared to those who completed the intervention (Table 1).

Twenty-three participants have completed the study procedures. The participants either did not need encouragement during the training to complete the sessions or were able to complete the training with a short and general encouragement statement (e.g., Well done, you can keep going, 2 min up to the training completion). In general, participants were satisfied with the CR (median-4, IQR: 3.5–5) and with the EVR as a platform for the training (median-4, IQR: 3.5–5), experienced being motivated by the intervention (median-4, IQR: 3–5), experienced cognitive progress through the intervention (median-4, IQR: 3.5–5) and expressed interest in taking part in similar interventions in the future (median-4, IQR: 3–5). Still, the experience of progress in everyday functioning following the intervention was average (Median-3, IQR: 2.5–5).

3.3. Preliminary efficacy of the intervention

A detailed report on the pre- and post-results and statistical analysis

Table 2
Pre- and post-intervention measurements and analysis of the differences (N = 23).

		Pre -Mean (SD)	Post -Mean (SD)	Differences: t	p	ES (r)
ASAP	Diversity	16 (4.92)	18.9 (7.36)	−2.9*	0.049	−0.22
	Frequency	2.71 (0.65)	2.54 (0.74)	1.16	>0.05	0.13
	Enjoyment	3.6 (0.7)	3.27 (0.81)	−1.7	>0.05	0.14
	Satisfaction	3.37 (0.86)	3.4 (0.89)	−0.2	>0.05	−0.02
OTDL-R		9.61 (4.83)	12.78 (6.56)	3.36-*	0.003	0.27-
TMT A		57.54 (24.15)	41.64 (12.12)	2.59*	0.003	0.3
CFT		15.6 (2.56)	17.2 (3.55)	−2.29*	0.034	0.65-
FBT	Inhibition	0.71 (0.13)	(0.11) 0.89	6.58-***	< 0.001	0.5-
		Median (IQR)	Median (IQR)	Wilcoxon (Z)	p	ES
COGNISTAT	Orientation	12 (10−12)	12 (11−12)	1.51-	0.13	0.13-
	Attention	7 (6–8)	8 (6–8)	1.2-	0.23	0.14-
	Language comprehension	5 (5–6)	6 (6–6)	1.51-	0.131	0.23-
	Visuomotor organization	4 (2–6)	6 (4–6)	1.96-*	0.05	0.25-
	Memory	11 (8–12)	10 (7–12)	0.43-	0.668	0.04-
	Similarities	7 (5–8)	8 (6–8)	1.65-	0.098	0.21-
	Judgment	6 (3–6)	6 (3–6)	0.1-	0.924	0.01
TMT B		132 (87–177)	96 (74–130)	2.78-*	0.006	0.27
PANSS	Positive symptoms	18 (14–23)	10 (8–18)	4.02-*	< 0.001	0.5
	Negative symptoms	14 (12–22)	11 (8–14)	3.94-*	< 0.001	0.3
	General psychopathology	35 (26–46)	23 (19–28)	3.89-*	< 0.001	0.38
	Total score	71 (60–96)	44 (39–56)	4.1-*	< 0.001	0.45
	Multi-tasking	0.98 (0.940–0.99)	0.99 (0.97–0.99)	2.02-*	0.044	0.55-
FBT	Persistence	0.83 (0.73–0.78)	0.96 (0.92–1)	3.77-*	< 0.001	0.45-
	Spatial-memory	0.82 (0.74–0.85)	0.89 (78–96)	2.6-*	0.009	0.27-
	Shifting-matching	0.75 (0.67–0.82)	0.79 (0.75–0.85)	1.23-	0.218	0.1-

Note: ASAP – Adults Subjective Assessment of Participation; CFT – Category Fluency Test; FBT – Functional Brain Trainer; COGNISTAT – Neuro Cognitive State Examination; OTDL-R – Observed Tasks of Daily Living Revised; PANSS – Positive and Negative Syndrome Scale; TMT A& B – Trail Making Test.
* $p < .05$
*** $p < .001$

by the 4 levels of training benefits is presented in Table 2.

3.3.1. Intervention engagement

Was confirmed, with medium to large effect sizes ($0.27 < r < 0.55$) demonstrating improvement on all evaluation tasks of the FBT software: multi-tasking, inhibition, initiation & persistence, and visual working memory.

3.3.2. Near transfer

We found improvements in standard, non-computerized cognitive assessments (COGNISTAT, CFT, TMT) following the intervention. Specifically, statistically significant improvement with medium effect size was seen in processing speed (TMT-A; ES = 0.38), cognitive flexibility (TMT—B; ES = 0.27), verbal fluency (CFT; ES = 0.25), and visual-motor organization (COGNISTAT subtest; ES = 0.25). No improvement was found in the memory and attention sub-tests of the COGNISTAT. Changes in abstract thinking and language comprehension (sub-tests of the COGNISTAT) had medium effect sizes (0.21 < ES < 0.23), but did not reach statistical significance.

3.3.3. Far transfer

A statistically significant improvement with medium to large effect size was found in functional capacity (OTDL-R; ES(r) = 0.27) and for all types of schizophrenia symptoms (measured using the PANSS): positive, negative, and general psychopathology (0.3 < ES(r) < 0.5).

3.3.4. Ecological transfer

A significant increase with medium effect size was indicated in participation diversity (ASAP; ES(r) = 0.22). No statistically significant improvement or decrement was found in other dimensions of participation (see Table 2).

3.4. Exploratory analyses: Association between improvement rates and demographic variables

No differences in outcome measures were found by gender and employment status (working/not working before the hospitalization) ($36.5 < U < 64$, $p > .05$), nor with previous experience with VR ($43 < U < 66$, $p > .05$). In addition, there was no correlation between the improvement rates in the cognitive, functional, and participation indices and all demographic variables (age, education, years of illness, age of illness onset and the hospitalization duration; $-0.36 < r < 0.414$, $p > .05$).

We further examined in a very exploratory way, whether improvement rates in the intervention engagement outcomes were associated with improvements in the near, far, and ecological transfer outcomes. We found that the improvement rates on engagement measures of FBT working memory and initiation and persistence were positively correlated with moderate strength with the extent of near transfer—improvement in the judgment (COGNISTAT), processing speed (TMT-A), and cognitive flexibility (TMT—B), and with the extent of the far transfer—general psychopathology ($0.41 < r < 0.52$, $p < .05$), but not with functional capacity nor with participation ($0.15 < r < 0.32$, $p > .05$). Finally, no correlation was found between the improvement rates of symptoms (PANSS; positive, negative and general) and participation indices ($-0.3 < r < 0.21$, $p > .05$), functional capacity ($-0.35 < r < 0.3$, $p > .05$), non-computerized cognitive assessments ($-0.43 < r < 0.36$, $p > .05$), and FBT scores ($-0.37 < r < 0.32$, $p > .05$). The only exceptions are an association of moderate strength between improvement in negative symptoms and abstract thinking ($r = 0.48$, $p < .05$), and in general psychopathology and self-initiation and persistence ($r = 0.47$, $p < .05$).

4. Discussion

This pilot study demonstrates the feasibility of a short, ecological, VR-based cognitive remediation applied in acute psychiatric wards in individuals with psychotic disorders. In addition, the results suggest a preliminary confirmation of the contribution of CR-EVR to improvement in cognitive functioning, functional capacity, and participation in daily life activities. Thus, the results address the potential of such an intervention approach for near and far transfer, but, importantly, for ecological transfer to daily life activities implying clinical benefits of CR-EVR in these settings.

4.1. Feasibility

The feasibility of the intervention was primarily indicated by a 25.8 % drop-out rate. While this rate is higher than the average attrition rate of 14.37 % (±13.8) for community-based CR interventions, it falls within the large range observed in previous CR studies (0–58 %; Vita et al., 2023) and the range for non-pharmacological interventions in schizophrenia (4–71 %; Szymczynska et al., 2017). Previous literature suggests that dropout rates in inpatient settings should be lower than those in community-based studies (Vita et al., 2023). However, studies focusing on acute mental health settings are rare, addressing mostly individuals with recent onset (Wykes et al., 2011), chronic hospitalization (e.g., Lu et al., 2012), or specific contexts as for hospital policies and practices (e.g., Gharaeipour and Scott, 2012) making it challenging to establish drop-out standards for such setting. The literature suggests that acute inpatient stays of short- to middle-length are often characterized by motivational challenges, positive symptoms exacerbation, and difficulties to adhere the treatment (Johnson et al., 2022). These factors may collectively contribute to drop-out and reduced compliance rates, as is supported by our findings showing some differences in the period of hospitalization between completers vs. drop-outs. The acceptable completion rate in our study may be attributed to the ecological content of the tasks, which connected the training to daily life functioning (Vita et al., 2023), and to experiencing satisfaction with the intervention, achieved progress, and motivation during the intervention (Szymczynska et al., 2017) as was reported by the participants in the post-intervention survey. This is despite the generally low level of staff involvement through the intervention in comparison to previous studies with inpatients (Ahmed et al., 2015; Tsapekos et al., 2019). However, it is noteworthy that participants who dropped out had no prior exposure to VR technology, suggesting that VR training may be more suitable for individuals with prior familiarity with technology.

4.2. Benefits of cognitive remediation through ecological VR platform

The basic level of the CR-EVR benefit was evident through improvement in trained tasks, indicating participant engagement in the intervention. Next, following the CR-EVR training, improvements were observed in near-transfer outcomes of the speed of processing, cognitive flexibility, and visuomotor skills, as measured by standard tools. These cognitive domains have consistently been found to be enhanced by CR (Fitapelli and Lindenmayer, 2022; Vita et al., 2021; Lejeune et al., 2021), including in inpatients with schizophrenia (Tsapekos et al., 2019). In addition, the near transfer may be accounted for by the similarity between training and evaluation modality: the training was visual, aimed at enhancing visual cognitive skills, and most of the cognitive assessments were visual as well. Moreover, prior research has found that CR tends to yield more favorable outcomes in the presence of a human therapist during the training sessions (Bowie et al., 2020; Fitapelli and Lindenmayer, 2022; Kambeitz-Ilankovic et al., 2019; Lejeune et al., 2021; Vita et al., 2021), a condition consistent with the approach taken in the current study. Notably, despite the visual nature of the intervention, we observed improvement in verbal speed of processing. This supports previous suggestions about possible transfer between the modalities (Scoriels et al., 2020). The features of the computerized training, including interactivity, ongoing feedback, and task-switching, likely contributed to the near-transfer. For example, each game switch during training provided additional opportunities for practicing shifting skills, thus, expanding the intervention dose. Still, the change was detected using tools that were shown to be highly sensitive to change in schizophrenia (Nuechterlein et al., 2023; Lipskaya-Velikovsky et al., 2016). Tests for attention and memory that were used in this study reached a ceiling effect, thus, their sensitivity to change was low, suggesting that, hypothetically, additional cognitive skills might be improved through the intervention.

We also observed medium-to-high effects in changes in schizophrenia symptoms and functional capacity measures. Of note, these results should be interpreted cautiously due to the lack of a control group, making it difficult to attribute the changes solely to the intervention. Still, previous evidence suggests the potential impact of CR on symptom alleviation (e.g., Scoriels et al., 2020). Importantly, it was observed that the degree of symptom relief showed little correlation with rates of change in the majority of study outcomes, suggesting in line with the previous literature (Harvey et al., 2019) that symptom relief may have a little contribution to some outcomes, such as functional capacity and participation. The finding showing the contribution of CR-EVR to the functional capacity improvement is in line with mounting evidence on the reliance of functional capacity on cognition (Harvey et al., 2019; Green et al., 2015; DeTore et al., 2019; Flores et al., 2022) and the potency of ecological tasks and environments simulation in provoking genuine responses in motivating ecological context advancing transfer (Sekhon et al., 2017). Moreover, there is little likelihood of its improvement with treatment as usual in hospital restrictive environments (Gupta et al., 2012; Harvey et al., 2019). Still, no association was found between the levels of intervention engagement and the extent of change in functional capacity. These findings may provide an additional demonstration of the fact that changes in functional capacity depend on multiple factors, including the degree to which the personal functional capacity is ingrained and solidified, in addition to engagement with the cognitive intervention. However, further research with larger sample sizes and with follow-up measurement points is needed to expand our understanding of the interplay between intervention engagement and functional capacity improvement.

Finally, we found ecological transfer following the intervention, which was demonstrated by an increase in the variety of participated activities. These offer initial evidence for the ecological validity of the CR-EVR. Such improvements may stem from the training platform features representing daily life tasks and environments. The results align with studies demonstrating, for example, the contribution of the CR to starting employment or to more general aspects of independent living (Lindenmayer et al., 2008; Wykes et al., 2011). Our results showing no decline in participation intensity (frequency), satisfaction, and enjoyment in restrictive inpatient settings may be positive outcomes for this population given the inpatient circumstances (Bowie et al., 2020). Alternatively, the lack of change in participation intensity might reflect the impact of the inpatient environment on activity patterns, which often predefines the frequency of certain activities (Krupa et al., 2016), e.g., you can do shopping only when you are on vacation, but not as frequent as you choose. Still, different rates of improvement in cognitive and functional capacity and participation further delineate the existing gap between these entities (Harvey et al., 2019; Fitapelli and Lindenmayer, 2022; Bowie et al., 2020). In addition, the findings may suggest a primary influence of CR on objective participation dimensions, but not on the subjective dimensions of enjoyment and satisfaction. These findings refute the assumption that relief in objective hindering factors will proliferate subjective experience with participation.

4.3. Study limitations

The study has several limitations which should be addressed in follow-up studies. The absence of a comparison group, either passive or active, limits our ability to definitively attribute the observed improvements to the CR-EVR intervention, as they may also be influenced by other treatments received during inpatient hospitalization. The relatively small sample size, coupled with the large number of outcome measures, may have increased the likelihood of inflated test significance. On the other hand, some statistical tests may fail to reach significance due to the small sample size employed; this is especially true in the case of the correlational analyses between symptoms' improvement rate and additional study variables, which ranged between −0.43 and 0.36, but still did not reach statistical significance. Near transfer on some of the trained components, such as self-initiation and persistence, was not assessed using standardized cognitive measurements. Future studies should aim to assess these aspects as well. Furthermore, the COGNISTAT, the test used as the standard evaluation of cognitive functioning, is a screening tool. Therefore, it provides only a brief estimation of cognitive functioning, which limits the generalizability of the results. Some of the tasks of the functional capacity test—the OTDL-R, which was used for the far transfer detection, are less common or outdated in today's world. Even though participation was measured in daily life occupations, we acknowledge that the person may still need to perform accommodations to carry out the occupations during the hospitalization (i.e., coordinate outings with the staff, arrange the activities for weekends and afternoon, take into account the department's schedule, etc.) in comparison to daily life. Thus, the gap may be assumed between the results of the participation measure and the actual participation after discharge. The lack of follow-up assessments precludes understanding of the long-term effects and sustained ecological validity of the improvements observed. Future research should address these issues to enhance our understanding of mechanisms and tools for participation enhancement; as well as demonstrate improvement in the outcome measures in terms of minimal clinically important difference and investigate characteristics of a population that will benefit from CR, including demographics, since some comparisons within current cohort were less informative given differences in the size of the groups, as in the case of gender.

4.4. Conclusions

To summarize, this pilot study shows the feasibility of a short-term, virtual reality-based cognitive remediation in a short-stay acute inpatient setting, demonstrating the potential for adherence, inpatient satisfaction, and engagement. The study suggests that training in ecological environments may enhance cognitive gains at various levels, benefiting functional capacity and daily life participation in individuals with schizophrenia and overcoming hindering factors for clinical implications. The findings indicate the potential of the sub-acute stage of psychiatric illness for cognitive enhancement. Future studies should incorporate these considerations to better understand the mechanisms and tools necessary for enhancing participation among individuals with schizophrenia.

CRediT authorship contribution statement

Reut Komemi: Writing – original draft, Methodology, Data curation. **Hana Tubenbaltt:** Data curation. **Eiran V. Harel:** Data curation. **Mor Nahum:** Writing – review & editing, Writing – original draft, Validation, Supervision. **Lena Lipskaya-Velikovsky:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Conceptualization.

Declaration of competing interest

None for all the authors.

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Trial registration depository: https://my.health.gov.il/CliniTrials/Pages/Home.aspx

Registration number: MOH_2019-08-19_007331.

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References

Ahmed, A.O., Hunter, K.M., Goodrum, N.M., Batten, N.J., Birgenheir, D., Hardison, E., Buckley, P.F., 2015. A randomized study of cognitive remediation for forensic and mental health patients with schizophrenia. J. Psychiatr. Res. 68, 8–18.

Attkisson, C.C., Greenfield, T.K., 1999. The UCSF client satisfaction scales: I. The client satisfaction questionnaire-8. In: Maruish, M.E. (Ed.), The Use of Psychological Testing for Treatment, Planning and Outcome Assessments, 2nd ed. Lawrence Erlbaum Associates, Mahwah, NJ, pp. 1333–1346.

Boland, R., Verduin, M., 2021. Kaplan & Sadock's Concise Textbook of Clinical Psychiatry. Wolters Kluwer.

Bowie, C.R., Leung, W.W., Reichenberg, A., McClure, M.M., Patterson, T.L., Heaton, R.K., Harvey, P.D., 2008. Predicting schizophrenia patients' real-world behavior with specific neuropsychological and functional capacity measures. Biol. Psychiatry 63 (5), 505–511. https://doi.org/10.1016/j.biopsych.2007.05.022.

Bowie, C.R., Bell, M.D., Fiszdon, J.M., Johannesen, J.K., Lindenmayer, J.P., McGurk, S. R., Medalia, A.A., Penadés, R., Saperstein, A.M., Twamley, E.W., Ueland, T., Wykes, T., 2020. Cognitive remediation for schizophrenia: an expert working group white paper on core techniques. Schiz Res 215, 49–53. https://doi.org/10.1016/j.schres.2019.10.047.

Brydges, C.R., 2019. Effect size guidelines, sample size calculations, and statistical power in gerontology. Innov. Aging 3 (4), 1–8. https://doi.org/10.1093/geroni/igz036.eCollection 2019 Aug.

Cella, M., Price, T., Corboy, H., Onwumere, J., Shergill, S., Preti, A., 2020. Cognitive remediation for inpatients with psychosis: a systematic review and meta-analysis. Psychol. Med. 50 (7), 1062–1076. https://doi.org/10.1017/S0033291720000872.

DeTore, N.R., Mueser, K.T., Byrd, J.A., McGurk, S.R., 2019. Cognitive functioning as a predictor of response to comprehensive cognitive remediation. J. Psychiatr. Res. 113, 117–124. https://doi.org/10.1016/j.jpsychires.2019.03.012.

Diehl, M., Willis, S.L., Schaie, K.W., 1995. Everyday problem solving in older adults: observational assessment and cognitive correlates. Psychol. Aging 10 (3), 478–491. https://doi.org/10.1037/0882-7974.10.3.478.

Fitapelli, B., Lindenmayer, J.P., 2022. Advances in cognitive remediation training in schizophrenia: a review. Brain Sci. 12 (2) https://doi.org/10.3390/brainsci12020129.

Flores, A.T., Hogarty, S.S., Mesholam-Gately, R.I., Barrio, C., Keshavan, M.S., Eack, S.M., 2022. Cognitive gains as a mechanism of functional capacity improvement in schizophrenia: results from a multi-site randomized controlled trial. J. Psychiatr. Res. 151, 554–560. https://doi.org/10.1016/j.jpsychires.2022.05.016.

Gaudino, E.A., Geisler, M.W., Squires, N.K., 1995. Construct validity in the trail making test: what makes part B harder? J. Clin. Exp. Neuropsychol. 17 (4), 529–535. https://doi.org/10.1080/01688639508405143.

Gharaeipour, M., Scott, B.J., 2012. Effects of cognitive remediation on neurocognitive functions and psychiatric symptoms in schizophrenia inpatients. Schiz Res 142 (1–3), 165–170. https://doi.org/10.1016/j.schres.2012.09.018.

Granholm, E., Holden, J.L., Mikhael, T., Link, P.C., Swendsen, J., Depp, C., Harvey, P.D., 2020. What do people with schizophrenia do all day? Ecological momentary assessment of real-world functioning in schizophrenia. Schizophr. Bull. 46 (2), 242–251.

Green, M.F., Llerena, K., Kern, R.S., 2015. The "right stuff" revisited: what have we learned about the determinants of daily functioning in schizophrenia? Schiz Bull 41 (4), 781–785. https://doi.org/10.1093/schbul/sbv018.

Gupta, M., Holshausen, K., Mausbach, B., Patterson, T.L., Bowie, C.R., 2012. Predictors of change in functional competence and functional behavior after functional adaptation skills training for schizophrenia. J. Nerv. Ment. Dis. 200 (8), 705–711. https://doi.org/10.1097/NMD.0b013e3182613f79.

Harvey, P.D., McGurk, S.R., Mahncke, H., Wykes, T., 2018. Controversies in computerized cognitive training. Biol Psychiatry Cogn Neurosci Neuroimag 3 (11), 907–915. https://doi.org/10.1016/j.bpsc.2018.06.008.

Harvey, P.D., Strassnig, M.T., Silberstein, J., 2019. Prediction of disability in schizophrenia: symptoms, cognition, and self-assessment. J. Exp. Psychopathol. 10 (3), 204380871986569.

Harvey, P.D., Bosia, M., Cavallaro, R., Howes, O.D., Kahn, R.S., Leucht, S., Vita, A., 2022. Cognitive dysfunction in schizophrenia: an expert group paper on the current state of the art. Schizophr Res Cogn 29, 100249.

Humm, L.B., Olsen, D., Morris, B.E.L.L., Fleming, M., Smith, M., 2014. Simulated job interview improves skills for adults with serious mental illnesses. Stud. Health Technol. Inform. 199, 50–54.

Jahn, F.S., Skovbye, M., Obenhausen, K., Jespersen, A.E., Miskowiak, K.W., 2021. Cognitive training with fully immersive virtual reality in patients with neurological and psychiatric disorders: a systematic review of randomized controlled trials. Psychiatry Res. 300, 113928 https://doi.org/10.1016/j.psychres.2021.113928.

Jarus, T., Barnea, R., Wasserlauf, N., Boretz, L.B., Yekuel, S., Galon, I., Peleg, L., Greenbaum, S., 2006. The Israeli assessment of participation for adults. Isr J Occup Ther 15 (2), H93–H111.

Johnson, S., Dalton-Locke, C., Baker, J., Hanlon, C., Salisbury, T.T., Fossey, M., Lloyd-Evans, B., 2022. Acute psychiatric care: approaches to increasing the range of services and improving access and quality of care. World Psychiat 21 (2), 220–236. https://doi.org/10.1002/wps.20962.

Kambeitz-Ilankovic, L., Betz, L.T., Dominke, C., Haas, S.S., Subramaniam, K., Fisher, M., Vinogradov, S., Koutsouleris, N., Kambeitz, J., 2019. Multi-outcome meta-analysis (MOMA) of cognitive remediation in schizophrenia: revisiting the relevance of human coaching and elucidating interplay between multiple outcomes. Neurosci. Biobehav. Rev. 107, 828–845. https://doi.org/10.1016/j.neubiorev.2019.09.031.

Kay, S.R., Opler, L.A., Lindenmayer, J.P., 1988. Reliability and validity of the positive and negative syndrome scale for schizophrenics. Psychiatry Res. 23 (1), 99–110. https://doi.org/10.1016/0165-1781(88)90038-8.

Kizony, R., 2018. Virtual reality for cognitive rehabilitation. In: Josman, N., Rosenblum, S., Katz, N. (Eds.), Cognition*, Occupation,* and p*articipation across the Life Span: Neuroscience*, Neurorehabilitation, and m*odels of Intervention*, 4th ed. AOTA Press, Bethesda, pp. 231–242.

Krupa, T., Kirsh, B., Pitts, D., Fossey, E.M., 2016. Bruce & borg's Psychosocial Frames of Reference: Theories, Models and Approaches for Occupation-Based Practice, 4th ed. Slack Incorporated.

La Paglia, F., La Cascia, C., Rizzo, R., Sanna, M., Cangialosi, F., Sideli, L., Francomano, A., Riva, G., La Barbera, D., 2016. Virtual reality environments to rehabilitation attention deficits in schizophrenic patients. Annu Rev Cyber Ther Telemed 14, 143–148.

Lejeune, J.A., Northrop, A., Kurtz, M.M., 2021. A Meta-analysis of cognitive remediation for schizophrenia: efficacy and the role of participant and treatment factors. Schizophr. Bull. 47 (4), 997–1006. https://doi.org/10.1093/schbul/sbab022.

Lindenmayer, J.P., McGurk, S.R., Mueser, K.T., Khan, A., Wance, D., Hoffman, L., Xie, H., 2008. A randomized controlled trial of cognitive remediation among inpatients with persistent mental illness. Psychiatr. Serv. 59 (3), 241–247. https://doi.org/10.1176/appi.ps.59.3.241.

Lipskaya-Velikovsky, L., Jarus, T., Easterbrook, A., Kotler, M., 2016. Participation in daily life of people with schizophrenia in comparison to the general population. Can. J. Occup. Ther. 83 (5), 297–305. https://doi.org/10.1177/0008417416647158.

Lipskaya-Velikovsky, L., Jarus, T., Kotler, M., 2017. Prediction of the intensity and diversity of day-to-day activities among people with schizophrenia using parameters obtained during acute hospitalization. Disabil. Rehabil. 39 (13), 1300–1306. https://doi.org/10.1080/09638288.2016.1194896.

Lu, H., Li, Y., Li, F., Jiao, X., Shi, W., Guo, K., Liu, P., 2012. Randomized controlled trial on adjunctive cognitive remediation therapy for chronically hospitalized patients with schizophrenia. Shanghai Arch Psychiatr 24 (3), 149–154. https://doi.org/10.3969/j.issn.1002-0829.2012.03.004.

McCutcheon, R.A., Keefe, R.S., McGuire, P.K., 2023. Cognitive impairment in schizophrenia:etiology, pathophysiology, and treatment. Mol. Psychiatry 28 (5), 1902–1918. https://doi.org/10.1038/s41380-023-01949-9.

Mitrushina, M., Abara, J., Blumenfeld, A., 1994. Aspects of validity and reliability of the neurobehavioral cognitive status examination (COGNISTAT) in assessment of psychiatric patients. J. Psychiatr. Res. 28 (1), 85–95. https://doi.org/10.1016/0022-3956(94)90037-x.

Mucci, A., Galderisi, S., Gibertoni, D., Rossi, A., Rocca, P., Bertolino, A., Del Favero, E., 2021. Factors associated with real-life functioning in persons with schizophrenia in a 4-year follow-up study of the Italian network for research on psychoses. JAMA Psychiatry 78 (5), 550–559. https://doi.org/10.1001/jamapsychiatry.2020.4614.

Nuechterlein, K.H., Green, M.F., Kern, R.S., 2023. The MATRICS consensus cognitive battery: an update. Curr. Top. Behav. Neurosci. 63, 1–18. https://doi.org/10.1007/7854_2022_395.

Parlar, M.E., Heinrichs, R.W., 2021. Cognitive decline and impairment in schizophrenia spectrum disorders reconsidered. Schizophr. Res. 228, 626–632. https://doi.org/10.1016/j.schres.2020.11.020.

Perra, A., Riccardo, C.L., De Lorenzo, V., De Marco, E., Di Natale, L., Kurotschka, P.K., Preti, A., Carta, M.G., 2023. Fully immersive virtual reality-based cognitive remediation for adults with psychosocial disabilities: a systematic scoping review of methods intervention gaps and meta-analysis of published effectiveness studies. Int. J. Environ. Res. Public Health 20 (2). https://doi.org/10.3390/ijerph20021527.

Plechatá, A., Hejtmánek, L., Bednářová, M., Fajnerová, I., 2021. Cognitive remediation in virtual environments for patients with schizophrenia and major depressive disorder: a feasibility study. Int. J. Environ. Res. Public Health 18 (17), 9081. https://doi.org/10.3390/ijerph18179081.

Scoriels, L., Genaro, L.T., Mororó, L.G.C., Keffer, S., Guimarães, A.L.D.V., Ribeiro, P.V.S., Tannos, F.M., Novaes, C., França, A.I., Goldenstein, N., Sahakian, B.J., Cavalcanti, M.T., Fisher, M., Vinogradov, S., Panizzutti, R., 2020. Auditory versus visual neuroscience-informed cognitive training in schizophrenia: effects on cognition, symptoms and quality of life. Schizophr. Res. 222, 319–326. https://doi.org/10.1016/j.schres.2020.05.017.

Sekhon, M., Cartwright, M., Francis, J.J., 2017. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. BMC Health Serv. Res. 17 (1), 88. https://doi.org/10.1186/s12913-017-2031-8.

Sheffield, J.M., Karcher, N.R., Barch, D.M., 2018. Cognitive deficits in psychotic disorders: a lifespan perspective. Neuropsychol. Rev. 28 (4), 509–533. https://doi.org/10.1007/s11065-018-9388-2.

Shochat, G., Maoz, S., Stark-Inbar, A., Blumenfeld, B., Rand, D., Preminger, S., Sacher, Y., 2017, June. Motion-based virtual reality cognitive training targeting executive functions in acquired brain injury community-dwelling individuals: A feasibility and initial efficacy pilot. In: In *2017 International Conference on Virtual Rehabilitation (ICVR*). IEEE, pp. 1–8.

Spreen, O., Strauss, E., 1998. Trail making test. A compendium of neuropsychological tests. Adm Norms Comment 2, 533–547.

Szymczynska, P., Walsh, S., Greenberg, L., Priebe, S., 2017. Attrition in trials evaluating complex interventions for schizophrenia: systematic review and meta-analysis. J. Psychiatr. Res. 90, 67–77. https://doi.org/10.1016/j.jpsychires.2017.02.009.

Tsapekos, D., Taylor, R., Cella, M., 2019. Feasibility and acceptability of brief cognitive remediation targeting metacognition in acute inpatients with psychosis: a case series. Neuropsychol. Rehabil. 29 (3), 361–375. https://doi.org/10.1080/09602011.2017.1301263.

Vita, A., Barlati, S., Ceraso, A., Nibbio, G., Ariu, C., Deste, G., Wykes, T., 2021. Effectiveness, core elements, and moderators of response of cognitive remediation for schizophrenia: a systematic review and meta-analysis of randomized clinical trials. JAMA Psychiatr 78 (8), 848–858. https://doi.org/10.1001/jamapsychiatry.2021.0620.

Vita, A., Barlati, S., Ceraso, A., Deste, G., Nibbio, G., Wykes, T., 2023. Acceptability of cognitive remediation for schizophrenia: a systematic review and meta-analysis of randomized controlled trials. Psychol. Med. 53 (8), 3661–3671. https://doi.org/10.1017/S0033291722000319.

Vos, T., Abajobir, A.A., Abate, K.H., Abbafati, C., Abbas, K.M., Abd-Allah, F., Aboyans, V., 2017. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the global burden of disease study 2016. Lancet 390 (10100), 1211–1259.

World Health Organization, 2001. International classification of functioning, disability and health. ICF. World Health Organization. https://iris.who.int/handle/10665/42407.

Wykes, T., Huddy, V., Cellard, C., McGurk, S.R., Czobor, P., 2011. A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. Am. J. Psychiatry 168 (5), 472–485. https://doi.org/10.1176/appi.ajp.2010.10060855.