Remediation of cognitive deficit in neuropsychiatric disorders using virtual carousel task and episodic memory task

I Fajnerova, K Sedlakova, V Vorackova, A Dorazilova, L Hejtmanek, A Plechata, M Rodriguez, K Vlcek

National Institute of Mental Health (NIMH),
Topolová 748, 250 67 Klecany, CZECH REPUBLIC

iveta.fajnerova@nudz.cz

www.nudz.cz/en/

ABSTRACT

The impairment of cognitive functioning represents a characteristic manifestation in various neuropsychiatric disorders, such as schizophrenia (SZ). Previous studies demonstrated mild to severe deficit almost in all cognitive domains. Our results obtained in the virtual analogue of the carousel maze also demonstrate impairment of spatial memory and cognitive flexibility in schizophrenia patients. In addition, results of the episodic-like memory task (EMT) also support the hypothesis of episodic memory deficit in schizophrenia. The aim of the presented study is to improve these impaired cognitive functions using remediation methods based on similar methods in a complex virtual environment. The remediation plan will be presented together with preliminary data obtained in a small group of schizophrenia patients.

1. INTRODUCTION

Cognitive deficit is considered to be a characteristic and permanent manifestation accompanying schizophrenia (SZ) and related psychotic disorders, affecting several cognitive domains (Green et al, 2004). The profile of deficits in schizophrenia includes among others also attention, working memory, reasoning and processing speed. Common to these abilities is the role of prefrontal cortex (PFC). The impaired ability to identify context using task-relevant information stored in a working memory, involving PCF hypofunction, was also described in SZ. Similar observations have been done in various task-switching paradigms (Jamadar et al, 2010). Moreover episodic memory deficits dependent on hippocampal (HPC) function are well-established among individuals with SZ (Aleman et al, 1999), often linked to strategic memory failures. The core of complex cognitive deficits observed in schizophrenia could be the impairment of cognitive coordination (neural control of cell population activity in time and context) controlled by hippocampal and prefrontal cortex (Phillips and Silverstein, 2003). This presumption is supported by the fact that frontotemporal dysfunction was demonstrated in schizophrenia (Meyer-Lindenberg et al, 2005). In order to assess and possibly remediate spatial abilities focused on episodic memory and cognitive coordination, we designed a computer-based episodic memory task (adopted from Vlcek et al, 2006) and a virtual task-switching paradigm in dynamic environment (Fajnerova et al, 2015).

2. EXPERIMENT 1 – THE EPISODIC-LIKE MEMORY TEST (EMT)

2.1 Method

2.1.1 Participants. Sixty-five subjects (39 males and 27 females, group SZ) who met ICD-10 criteria for first psychotic episode of schizophrenia spectrum disorder (F20.X (n=4) and F23.1/F23.2 (n=32)). The healthy control subjects (N=100, 50 males and 50 females, group HC) were recruited from the same socio-demographic background via a local advertisement. The average age of both groups was 28 years (SZ: 28.8 ± 7.7; HC: 28.7 ± 9.1), and most of the participants in both groups had education level 4 (university).

2.1.2 Clinical assessment. To confirm the cognitive deficit in our study subjects, all participants (SZ and HC) completed a battery of standard cognitive tests (Trail-Making Test; Spatial Span (WMS-III); Rey-Osterrieth Complex Figure Test; Block Test (WAIS-III); Perceptual Vigilance Task (PEBL), Money-Road Map Test, Key Search Test). In addition, all patients were evaluated using the PANSS and GAF psychiatric scales to address the presence of clinical symptoms.

2.1.3 The non-verbal working memory form of the Episodic-like Memory Test (EMT). The computerized EMT test (previously published by Vlcek et al, 2006) is based on the concept of testing the memory for information about **'where'** a specific event (episode) took place, **'what'** occurred during this episode, and **'when'** it happened (Clayton and Dickinson, 1998). The test was adjusted in order to test the short-term memory for episodic events, consisting of a presentation and a testing phase (see Figure 1- left). In the presentation phase, the subject was shown a computer screen with several objects (pictures) in predefined places on the right part of the screen and an empty open box on the left. The tested person was instructed to drag the pictures from the predefined places in a given order into the chest, using the computer mouse. The subject was asked to memorize both the order and the position of each picture. After a short delay (of several seconds), in the following testing phase the subject was shown all the pictures dragged during the previous presentation phase to the box placed in one single row at the bottom of the screen in a pseudorandom order (see Fig.1). He/she was then asked to drag the pictures in the same order as they were dragged into the box to their correct position. The test is performed in three successive levels of difficulty: three, five and seven pictures of common objects. We evaluated separately two aspects of the information: errors in the "where" (position of the pictures) and "when" information (order of the pictures).

Figure 1. *EMT test: presentation phase and testing phase (left); The virtual Carousel maze task: Schematic view of the two reference frames - Room (square shape) and Arena frame (circular shape) and arena from the first-person view (right), adjusted according to [Fajnerova et al, 2015]*

2.2 Results

2.2.1 Cognitive assessment. The non-parametric Mann-Whitney U test showed impaired performance almost in all neuropsychological measures focused on learning and long-term memory, working memory, attention, processing speed and mental flexibility, executive functioning and specific spatial abilities (mental perspective taking). The detailed results are not presented (for details see Fajnerova et al, 2015).

2.2.2 EMT results. The repeated measures ANOVA showed significant group effect both in EMT position and order errors ($p < 0.0001$). Similarly, the difficulty level (number of pictures used during the test) had significant effect both in spatial and temporal component ($p < 0.0001$). However, the significant interaction effect (group x difficulty) was found only in the memory for ORDER, but not for POSITION (see Figure 2).

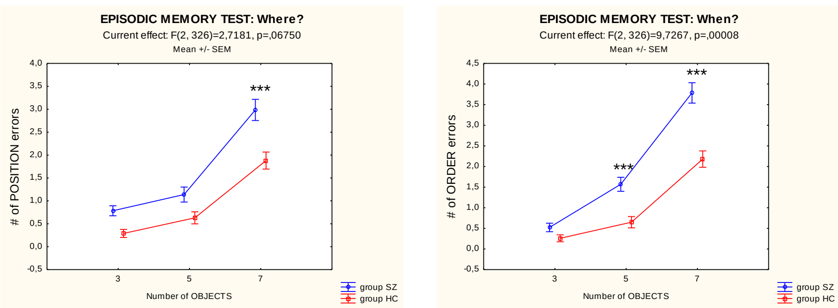

Figure 2. *EMT group results for both POSITION (left) and ORDER (right) errors (*** p < 0.001).*

3. EXPERIMENT 2 – VIRTUAL CAROUSEL MAZE TASK (ACTIVE ALLOCENTRIC PLACE PREFERENCE)

3.1 Method

3.1.1 Participants. A study group of 30 (17 males, age 18-35) first-episode schizophrenia patients (SZ, diagnosed as acute psychotic episode or schizophrenia according to DSM-IV) and a matched control group of healthy controls (HC, n=30) were recruited and matched for age, sex, education level and gaming experience.

3.1.2 Clinical assessment. All participants (SZ and HC) completed a battery of standard cognitive tests (for details see section 2.1.2).

3.1.3 Apparatus and software. The game engine Unreal Engine (Epic Games) was used to visualize the virtual scene to the respondents presented in a first-person view on a 24" LCD monitor. The custom-made java software toolkit called "SpaNav" was connected to the game engine to control the experiment and collect data. Subjects controlled their movement in the virtual environment using one joystick of the gamepad device.

3.1.4 Design and Procedure. Prior to the experiment all participants underwent a short pre-training of movement control in complex virtual maze. Consecutively all performed experiment in the virtual Carousel maze task, called also the Active Allocentric Place Preference task (AAPP, Fajnerova et al, 2015). The hidden goal principle was used to test spatial abilities in subjects standing on a rotating arena. The hidden goal positions were connected either 1) to the ARENA frame (rotating together with the subject) or 2) to the ROOM frame moving with respect to the subject/arena (see visible goals illustrated as circular or squared shapes in Fig. 1 on the right). The task was divided to four separate phases: *1) Training* - searching for two goals, one in the arena frame and one in the room frame; *2) Arena frame* - navigation towards two goals rotating with the arena and thus stable in respect to the position of the subject; *3) Room frame* - navigation towards two goals stable in room frame and thus moving in respect to the subject standing on the rotating arena; *4) Frame switching* - alternated search between 4 goals placed either in arena frame or in room frame. Each single trial started with pointing towards the goal and was followed by navigation (20s time limit) towards the goal using 3 visible orientation cues. The performance in the *Rotating arena* was measured using the *pointing error* parameter and the *trial time* parameter (time needed to enter the goal position). Only the data for the trial time parameter are presented in this paper as the most sensitive measure of behavioural impairment in schizophrenia.

3.2 Results

All phases of the virtual Carousel maze task showed decline of spatial performance in SZ: 1.*Training phase* showed impaired learning abilities ($p < 0.01$, Fig. 3A); 2. *Arena frame* showed mild impairment in navigation towards stable goals ($p < 0.01$) less expressed in the second half (Fig. 3B); 3.Room frame showed strongly impaired navigation towards the moving goals connected to the *Room frame* (Fig. 3C) showed strongly profound decline of spatial abilities in SZ ($p < 0.001$); 4. Frame-switching paradigm showed substantial deficit in SZ patients ($p < 0.001$, see Fig. 3D).

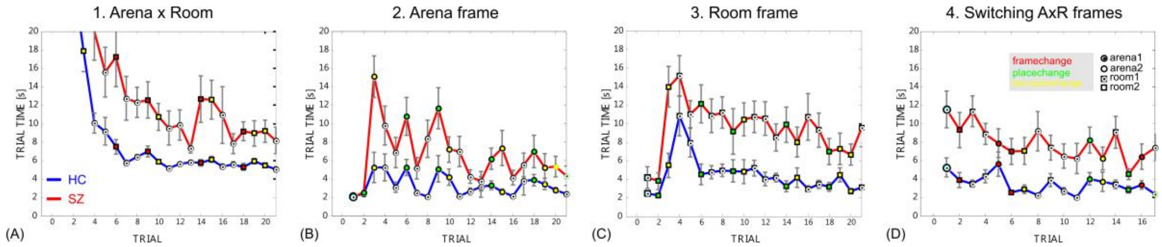

Figure 3. *(A-D) Group performance in four phases of the virtual Carousel maze task expressed using the Trial time parameter. (A) Training phase with simple frame switching (1arena x 1room). (B) Arena frame performance. (C) The Room frame performance. (D) Alternation between 4 previously acquired goals, placed in two reference frames; adopted from [Fajnerova et al, 2015].*

4. VIRTUAL REMEDIATION PROGRAM

Both tasks EMT and Carousel maze have a spatial component. We believe that such spatial tasks have the potential to assess cognitive performance in ecologically valid environments. Our aim is thus to apply similar methods in cognitive remediation program in SZ aimed at complex cognitive abilities:

A. **Episodic memory** – paradigm involving memorizing of objects position and order in complex virtual scenes (see Figure 4). The difficulty level can be increased in the course of the training program 1) by means of the number of objects that should be remembered (starting by 3 and increasing by 1 object after successful trials up to 10 objects), and 2) in the means of complexity of the virtual environment ranging from simple virtual rooms (e.g. offices or houses) to a large-scale environments of a small virtual city.

B. **Spatial memory and cognitive coordination** in a switching paradigm involving switching between spatial reference frames in dynamic environment of the Carousel maze. The training will take place in the following phases: 1) one goal position on a stable arena (without rotation); 2) switching between 2 goals on a stable arena; 3) two goals rotating together with the arena; 4) one goal attached to the room frame (requiring navigation towards the moving object) with no arena orientation cues as distractors; 5) one goal in the room frame with distracting arena cues; 6) two goal positions connected to the room frame; 7) two goals rotating with the arena and two goals connected to the room frame. Difficulty level can be also adjusted using increasing number of distracting orientation cues in the environment and the complexity of the environment outside the arena (ranging from room to complex city environment surrounding the rotating arena).

Figure 4. *Illustration of the Episodic memory (for position and order of several objects) training task in the virtual office environment. The arrow points towards the next object in the sequence that should be picked-up and remembered. On the bottom of the scene is the object inventory showing objects that should be later placed in the correct sequence back on the same locations. Objects in the inventory are randomized in the beginning of the recall phase.*

4. CONCLUSIONS

The presented results show significant deficit of spatial abilities in first episode schizophrenia patients, both in spatial memory and mental flexibility tested in dynamic environment of rotating arena, and episodic memory tested in simple computer task. As individual phases or difficulty levels of these tests demonstrate variable extent of sensitivity towards the cognitive deficit in SZ, we propose this tasks as suitable tools for virtual remediation of impaired visuo-spatial abilities and cognitive coordination in schizophrenia. Based on these results we propose a complex cognitive remediation in two virtual reality tasks enabling us easy manipulation with environmental stimuli that could help us to prevent boredom and increase the motivation of trained schizophrenia patients, and good control over the increasing difficulty level necessary for effective training.

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