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Differential diagnosis of schizophrenia and schizoaffective disorder from normal subjects using virtual reality

Mahmoud Kargar[a], Sajad Askari[b], Afshin Khoshaman[c], Alireza Mohammadi[d,*]

[a] Department of Speech Therapy, School of Rehabilitation, Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Urban Planning, Shiraz University, Shiraz, Iran
[c] Department of Architecture, Shiraz University, Shiraz, Iran
[d] Neuroscience Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

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ABSTRACT

Dysfunction of allocentric and egocentric memories is one of the core features of psychiatric disorders. There are a few navigational studies on these memories in schizophrenia and bipolar disorders, but studies in schizoaffective disorder are lacking. Here, we aim to explore allocentric and egocentric navigation deficits in these subjects using our advanced recently developed virtual reality navigation task (VRNT). Twenty patients with schizophrenia and 20 with schizoaffective disorder were compared with 20 normal volunteer subjects on VRNTs consisting of a virtual neighbourhood (allocentric memory) and a virtual maze (egocentric memory). Compared with schizoaffective disorder and control subjects, patients with schizophrenia had the worst performance on both virtual neighbourhood and virtual maze tasks. The allocentric memory in both patients with schizophrenia and those with schizoaffective disorder was more impaired than the egocentric memory ($p < 0.001$). However, the patients with schizoaffective disorder performed better in egocentric memory than those with schizophrenia, as they had fewer errors in the virtual maze. It was concluded that allocentric memory is more impaired than egocentric in both schizoaffective disorder and schizophrenia patients, whereas patients with schizoaffective disorder performed better in egocentric memory than patients with schizophrenia. It was also concluded that allocentric memory deficits can help differentiate patients with schizophrenia and schizoaffective disorder from healthy participants, whereas egocentric memory deficits can be used to distinguish them from each other.

1. Introduction

Schizophrenia is considered to be a neuropsychiatric disorder and results in delusions, hallucinations, progressive cognitive impairments, and disorganized behaviours (Mohammadi et al., 2018c, 2018a; van Os and Kapur, 2009), while schizoaffective disorder is characterised by a combination of schizophrenia and mood disorder symptoms, such as hallucinations or delusions, and depression or mania (Lake andHurwitz, 2007, 2006; Martin et al., 2007).

Kreapelin (1971)created a clear contrast between schizophrenia and mood disorders known as the Kraepelinian dichotomy. To describe patients who presented with mixed symptoms of schizophrenia and affective disorder, Kasanin (1994) introduced the term schizoaffective for the first time and stated that the long-term outcomes of schizoaffective disorder patients are better than those of schizophrenia patients and worse than those of mood disorder patients. Currently, there are continuing debates over whether schizoaffective disorder can suggest a diagnostic entity that could be biologically distinguished from schizophrenia (Gooding and Tallent, 2002; Kempf et al., 2005; Maj et al., 2000; Pope et al., 1980; Taylor, 1992). To clarify the differential diagnosis between schizoaffective disorder and schizophrenia, comparative neuropsychological studies may be helpful. While there is much evidence from neuropsychological investigations on schizophrenia and schizoaffective disorder indicating a broad range of cognitive impairments with focus on working memory, attention, and problem solving (Buchananet al., 2005; Gooding and Tallent, 2002; Hoff and Kremen, 2003; Kuperberg and Heckers,2000), there is little evidence of navigational deficits in patients with schizoaffective disorder. Currently, two main types of spatial navigation have been introduced: the allocentric representation (independent from the observer) and the egocentric representation (related to the axes of the body) (Barry et al., 2006; Mohammadi et al.,2018b; O'Keefe and Nadel, 1979).The allocentric representation (object- or environment-centered) allows a person to experience the world from an identical and more

* Corresponding author.
E-mail address: ar.mohammadi@bmsu.ac.ir (A. Mohammadi).

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impersonal viewpoint, whereas the egocentric memory (ego-centered or body-centered) provides a person the ability to comprehend the world from a personal perspective. The egocentric representation plays an important role in maintaining a stable moment-to-moment perception, while the allocentric representation is known by more familiarity with the environment (Barry et al., 2006; Mohammadi et al.,2018b; O'Keefe and Nadel, 1979). In the other words, egocentric representation refers to the capability to see the world from the personal view and presents a self-to-object representational pattern, while allocentric representation refers to the capability of experiencing the world from the indistinguishable and more impersonal view and presents an object-to-object representational pattern.

The evidence suggests that patients with schizoaffective disorder exhibit a pattern of cognitive impairments which is very similar to that observed in schizophrenia. The Voxel-based morphometry and functional magnetic resonance imaging (fMRI) studies have indicated that hippocampal volume similarly decreased in the patients with schizophrenia and schizoaffective disorder (Amann et al., 2016; Arnold et al., 2015; Haijma et al., 2013; Nelson et al., 1998; Radonić et al., 2011; Weiss et al., 2005). However, Weiss et al.(2005)have demonstrated that reduced hippocampal volume is extended through the frontal to posterior regions, and it is not limited to a specific region of the hippocampus. Furthermore, patients with schizoaffective disorder showed extensive regions of gray matter reduction similar to those observed in schizophrenia, whereas the patients with bipolar disorder did not (Amann et al., 2016; Arnold et al., 2015; Radonić et al., 2011). This finding suggests that patients with schizoaffective disorder are more similar to schizophrenic subjects than those with bipolar disorder.

It has been revealed that spatial navigation is associated with activation of parahippocampal gyrus, posterior hippocampus, striatum (caudate nucleus), the parietal and temporal lobes, and the prefrontal and retrosplenial cortices (Aguirre et al., 1996; Boccia et al., 2014; Bohbot et al., 1998; Burgess et al., 2001; Grön et al., 2000; Hartley et al., 2003; Iaria et al., 2003; Iglói et al., 2010; Maguire et al., 1997; Marsh et al., 2010; Mohammadi et al., 2018a, 2018b; Orban et al., 2006; Parslow et al., 2004; Peigneux et al., 2004; Rasetti et al., 2014; Rauchs et al., 2008; Shipman and Astur, 2008; Weniger and Irle, 2006; Xu et al., 2010). Interestingly, the reduced activation of the left occipital/temporal cortex and the left dorsolateral prefrontal cortex (DLPFC) during spatial navigation have been reported in the subjects with schizophrenia (Salgado-Pineda et al., 2016). Likewise, the reduced activation in the parahippocampal gyrus have been shown in the patients with schizophrenic. Recently, virtual spatial navigation tasks is used as a tool for distinguishing defects of allocentric and egocentric memories. Hence, the development of virtual reality technologies provided a great progression in the study of visuospatial navigation and memory by simulating a large environment in the first-person perspective. Many studies have investigated verbal and spatial working memories in patients with schizophrenia and schizoaffective disorder (Conklin et al., 2000; Fleminget al., 1995; Glahn et al., 2003; Gooding and Tallent, 2002; Hanlon et al., 2006; Kim et al., 2004; Park and Holzman, 1992), and spatial navigation in patients with schizophrenia (Agarwal et al., 2015; Mohammadi et al., 2018b; Weniger and Irle, 2008); however, studies on allocentric and egocentric memories in patients with schizoaffective disorder are lacking.

Our recently-developed virtual reality navigation task (VRNT) with two virtual environments was used in this study to explore allocentric (virtual neighbourhood) and egocentric (virtual maze) navigation deficits of patients with schizophrenia or schizoaffective disorder. Based on the interstitial status of schizoaffective disorder (with concurrent schizophrenia and mood disorder symptoms) and our previous findings, we hypothesised that schizoaffective disorder patients may have a better status than those with schizophrenia. We also examined whether there was a special categorical pattern of spatial navigation deficits among patients with schizophrenia and those with schizoaffective disorder.

2. Methods

2.1. Participants

Patients were recruited from outpatient services at Imam Hossein hospital (Tehran, Iran). The healthy group was selected by the diagnosis of neurologists and then by psychiatric specialists from hospital employees who voluntarily enrolled. No history of psychotic problems was found in the control group, and only those subjects with no history of additional neurological or psychiatric disease were included. All subjects signed a standard informed consent form approved by the local ethics committee. The VRNT performances of 60 subjects (average age = 39–41 years), including 20 with schizophrenia, 20 with schizoaffective disorder, and 20 cognitively normal controls, were compared. All subjects underwent a systematic selection process and were diagnosed by an expert psychiatrist based on DSM-IV diagnostic criteria. All subjects received a neuropsychological assessment. The Ethical Committee of the Baqiyatallah University of Medical Sciences approved the study design (No: IR.BMSU.REC.1396.14).

2.2. Procedure

First, neuropsychological assessments were carried out. Verbal, nonverbal, allocentric, and egocentric memories were assessed using Auditory-Verbal Learning Test (AVLT), Rey-Osterrieth Complex Figure Test (ROCFT-R), and our recently-designed VRNT, respectively. All of these assessments (from registering to the end of neuropsychological tests) were performed within 11 months.

2.3. Neuropsychological assessment

To examine the cognitive function of subjects, the neuropsychological assessment of all subjects was performed covering the following cognitive areas: (1) Verbal memory: Auditory-Verbal Learning Test (AVLT, sum of trials 1–5, recall after interference, delayed recall after 30 min, and memory recognition) (Rey, 1941; Schmidt, 1996), (2) Nonverbal memory: Rey-Osterrieth Complex Figure Test (ROCFT-R; recall condition, immediate) (Meyers and Meyers, 1995), (3) Visuospatial memory: Rey-Osterrieth Complex Figure Test (ROCFT-D; after 30 min delay)(Meyers and Meyers, 1995), and (4) Global cognitive function: the Folstein's Mini-Mental State Examination (MMSE) (Folstein et al., 1975).

2.4. Virtual reality environment task (VRNT)

2.4.1. Test design

The virtual reality environment techniques have been previously described and used as appropriate tools for evaluating visuospatial navigation abilities(Agarwal et al., 2015; Byagowi et al., 2014; Byagowi and Moussavi, 2012; Mohammadi et al., 2018a, 2018b; Waller and Lippa, 2007; Weniger and Irle, 2006, 2008). Our novel 3D first-person perspective virtual reality environment (virtual neighbourhood and virtual maze) was created using AutoCAD, Adobe Photoshop CS6, and Autodesk 3Ds Max software and run in the Lumion pro 5.0 editor. The virtual environment was designed in two versions, the virtual neighbourhood and the virtual maze, to evaluate allocentric and egocentric spatial navigation, respectively. The virtual neighbourhood consisted of several buildings and streets with a lot of landmarks through which subjects could navigate their way; the virtual maze consisted of walls and corridors with no landmarks, and subjects had to navigate their way based on their mental map.

A 15.6-inch laptop monitor was used to present the virtual environment to the subjects. Subjects moved through the virtual environments using four keys to move forward, backward, left, and right and a mouse to control head directions. First, the subject received 2D overhead view images of the virtual environment for 60 s (Fig. 1B and

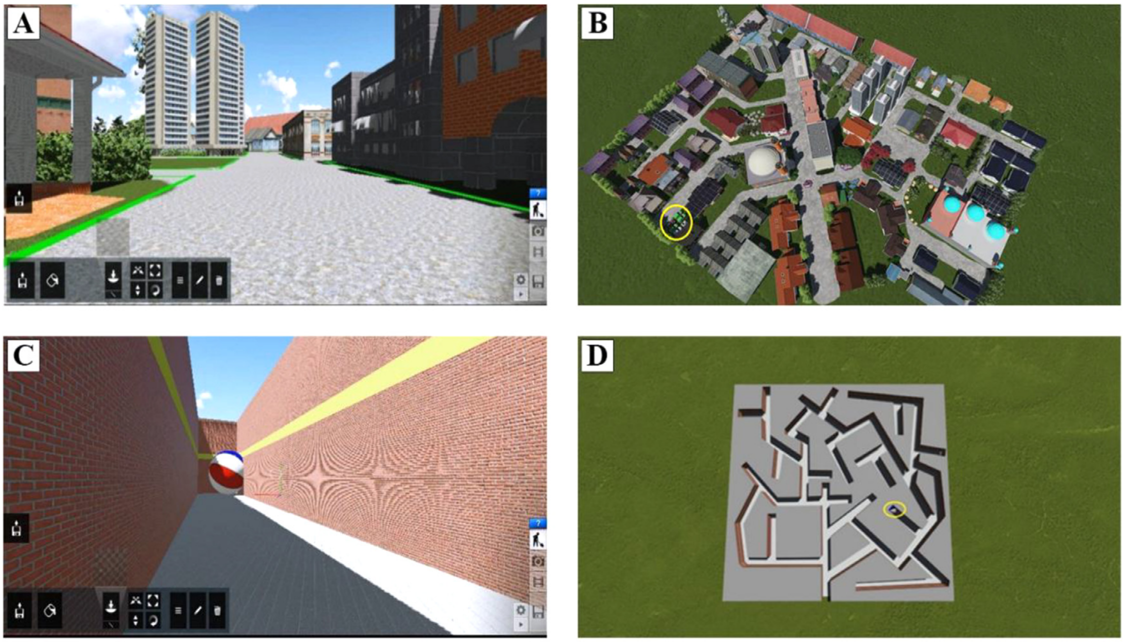

Fig. 1. Top: The first person view (A), and Overhead view (B) of the virtual neighbourhood; Bottom: The first person view (C), and Overhead view (D) of the virtual maze. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

D). Then he/she was asked to find the given goal [parking in the virtual neighbourhood and a ball in the virtual maze] in the 3D first-person view (Fig. 1A and C). In the first-person view of the virtual neighbourhood (Fig. 1A), the subject was instructed to find the location of a parking space marked in the 2D overhead-view image of the neighbourhood (yellow circle). In the first-person view of the virtual maze (Fig. 1C), the subject was instructed to find the location of a ball marked in the 2D overhead-view image of the maze (yellow circle). After receiving 3 trials and being familiar with the environment, the participants started the route from the entrance of 3D environment using a mouse to reach the goal in both tasks [parking in the virtual neighbourhood (Fig. 1A) and a ball in the virtual maze (Fig. 1C)] and the correct scores and time of completion of each trial were recorded. This paradigm was randomly transformed into five states (the status of the paradigm was rotationally different for each patient). Patients should be targeted based on two types of information. The location of the goal at the overhead view and the landmarks of the route in 3 training trials of the virtual neighbourhood (but not the virtual maze). In the virtual maze, the patient should find the goal by recalling the spatial map of the route. The landmarks have served as beacon-cues— a landmark that is very close to the goal location which enables the navigator closer to his or her goal. Subjects explored the virtual environment until they found their way and reached the given goal or until they felt sure that they could not find their way. Moreover, the start locations and the location of the given goal (parking in the virtual neighbourhood and a ball in the virtual maze) were different for any of the participants. After the completion of two virtual tasks and data collection, the data files were processed to produce primary data tables for further statistical analysis.

2.4.2. Scoring

In both virtual tasks, correct responses [The number of times reaching the goal (Parking and the ball) among 5 trials and the time spent in each trial to reach the goal] were measured. For each correct answer, one point was considered, and the sum of the correct answers was computed after 5 trials; the time of completion was also calculated for each trial. The response time and the number of correct responses were used as the dependent variables for further statistical analysis.

2.5. Statistical analysis

To compare the demographic variables, neuropsychological test scores, and performances of virtual environment tasks (virtual neighbourhood and virtual maze) of all groups, the one-way ANOVA test was administered. Differences of demographic variables among groups were analyzed using one-way ANOVA tests followed by post-hoc Tukey HSD test. Scores of neuropsychological tests and performance on the VRNT (correct responses and the time of response) were analyzed by one-way ANOVA tests. Statistical analyses were carried out by IBM SPSS Statistics v. 22.

3. Results

3.1. Descriptive statistics and neuropsychological test scores

Analysis of the demographic variables indicated that there were no differences in the age, years of education (almost all of participants were at the same level of education), handedness, or duration of the disorder among the groups ($p > 0.05$), but the MMSE score differed among the groups. The MMSE scores of the schizophrenia and schizoaffective groups were significantly lower than the scores of normal group ($p < 0.001$ and $p < 0.05$, respectively). The number of female participants in the schizophrenia and schizoaffective disorder groups was higher than the number of males (60% and 55%, respectively), while the control group had an equal number of men and women. The demographic characteristics of the participants can be seen in Table 1.

The analysis of neuropsychological scores showed significant between-group differences ($p < 0.001$). The results showed that schizophrenia subjects had poorer performances in all neuropsychological sub-tests than the normal subjects ($p < 0.001$). There was also a significant difference between schizoaffective disorder patients and schizophrenia subjects ($p < 0.05$). Analysis showed that schizoaffective disorder patients were significantly better than schizophrenia patients in RAVLT and ROCFT ($p < 0.05$). Similarly, patients with schizoaffective disorder had poorer performances than those in the control group on the RAVLT total, immediate recall, delayed recall, memory recognition, ROCFT immediate recall, and delayed recall scores (Table 2) ($p < 0.01$).

Table 1
Demographic characteristics of the groups.

Characteristics	Normal controls ($n = 20$)	Participants with schizophrenia ($n = 20$)	Participants with schizoaffective disorder($n = 20$)
Age (Year)	41.1 ± 4.5	40.55 ± 8.5	39.9 ± 2.673
MMSE	29.1 ± 1.02	27.5 ± 1.24***	28.64 ± 1.36*,##
Education (Year)	13.5 ± 2.47	12.8 ± 2.451	13 ± 2.316
Handedness (Right: Left)	18: 2	18: 2	17: 3
Sex (Female: Male)	11:9	13:7	11: 9
Duration of disorder (Year)	–	11.35 ± 3.679	10.15 ± 1.531
Extrapyramidal motor symptoms[a] (None: Mild: Moderate: Severe)	–	20: 0: 0: 0	20: 0: 0: 0
Medication type			
Neuroleptics			
Typical only		4	0
Atypical only		16	13
Both types		0	7
CPZ equivalents			
Mood stabilizers			
Lithium		0	3
Other		0	12
Antidepressants		3	9
Benzodiazepines		9	10
Anti-Parkinson agents		0	0
None (unmedicated)	–	0	0

MMSE, total score; Handedness, based on Edinburgh Handedness Inventory; NA, not applicable.
Values are mean ± SD.
[a] Symptoms included: Akathisia, Abnormal involuntary movements, Wrist rigidity, Tremor, Dystonia, and Tardive dyskinesia.
*** $p < 0.001$, statistical comparisons (ANOVA with Tukey HSD post hoc): to the normal group.
* $p < 0.5$, statistical comparisons (ANOVA with Tukey HSD post hoc): to the normal group.
$p < 0.01$, statistical comparisons (ANOVA with Tukey HSD post hoc): to the schizophrenia group.

3.2. Virtual reality navigation task (virtual neighbourhood, virtual maze)

In the virtual environment tasks, the number of correct answers and the time of completion of each trial were considered as dependent variables. All participants' response scores and response times were analyzed and compared. Analysis showed that there were significant differences among the groups in the virtual neighbourhood and virtual maze tasks (Table 3).

3.2.1. Virtual neighbourhood task

Comparing the sum of correct responses in 5 trials performed by patients with schizoaffective disorder, those with schizophrenia, and the control subjects in the virtual neighbourhood demonstrated that there were significant differences among the groups. Compared with the control group, the schizophrenia patients and the schizoaffective disorder patients performed worse in the virtual neighbourhood tasks ($p < 0.001$ and $p < 0.01$, respectively). Significant differences were observed between patients with schizoaffective disorder and those with schizophrenia in both number of correct responses and response time across all 5 trials ($p < 0.05$) (Table 3). The ANOVA results and effect size are presented in Table 4.

3.2.2. Virtual maze task

Compared with the control group, patients with schizophrenia had

Table 2
Neuropsychological characteristics of the groups.

Characteristics	Normal controls ($n = 20$)	Participants with schizophreni($n = 20$)	Participants with schizoaffective disorder($n = 20$)
RAVLT			
Total score:	48.45 ± 3.76	30.25 ± 6.75***	40.25 ± 2.173**,#
Immediate recall score	12.45 ± 1.205	4.64 ± 1.125***	7.7 ± 1.341**,#
Delayed recall score	9.45 ± 1.932	5.25 ± 1.545***	6.5 ± 1.317**,#
Memory recognition	14.56 ± 1.135	8.6 ± 1.25***	10.8 ± 1.239**,#
ROCFT			
Immediate recall score	11.65 ± 1.025	8.15 ± 1.125***	8.25 ± 1.019**,#
Delayed recall score	9.85 ± 1.165	6.5 ± 1.856***	7.35 ± 1.136**,#
PANSS total	–	62.19 ± 15.0	64.7 ± 13.3
PANSS positive	–	15.6 ± 4.6	16.7 ± 3.8
PANSS negative	–	15.6 ± 4.9	14.7 ± 3.9
YMRS	–	4.8 ± 4.4	6.5 ± 5.2
MADRS	–	8.3 ± 6.8	14.6 ± 9.3

NA, not applicable; The Rey Auditory Verbal Learning Test (RAVLT), RAVLT total scores, sum of trials 1 to 5; RAVLT immediate recall, recall after interference; RAVLT delayed, recall after 30 min; Memory recognition, total word remembered from presented words; ROCFT Immediate recall score, recall immediately; Rey–Osterrieth complex figure test (ROCF), ROCFT Delayed recall score: recall after 30 min; PANSS: Positive and Negative Syndrome scale; YMRS: Young Mania Rating Scale; MADRS: Montgomery-Åsberg Depression Rating Scale.
Values are mean ± SD.
*** $p < 0.001$, statistical comparisons (ANOVA with Tukey HSD post hoc): to the normal group.
** $p < 0.01$, statistical comparisons (ANOVA with Tukey HSD post hoc): to the normal group.
# $p < 0.05$, statistical comparisons (ANOVA with Tukey HSD post hoc): to the schizophrenia group.

Table 3
The performance of groups on virtual reality navigation task.

Test	Normal controls (n = 20)	Participants with schizophrenia (n = 20)	Participants with schizoaffective disorder(n = 20)
Virtual neighbourhood			
Mean correct response (5 trials)	4.63 ± 0.215	2.74 ± 0.516***	3.35 ± 0.67***,#
Mean response time (Sec)	61.42 ± 7.39	102.58 ± 11.312***	98.7 ± 16.502***,#
Virtual maze			
Mean correct response (5 trials)	4.44 ± 0.472	3.77 ± 0.787*	4.2 ± 0.767
Mean response time (Sec)	66.23 ± 17.27	87.94 ± 16.33*	80.71 ± 18.393*

Mean correct response, mean number of responses during 5 trials; mean response time, mean time that takes to find the goal during 5 trials.
Values are mean ± SD.
*** $p < 0.001$, statistical comparisons (ANOVA with Tukey HSD post hoc): to the normal group.
* $p < 0.5$, statistical comparisons (ANOVA with Tukey HSD post hoc): to the normal group.
# $p < 0.05$, statistical comparisons (ANOVA with Tukey HSD post hoc): to the schizophrenia group.

Table 4
The ANOVA results and effect size.

Variable	df	F	Sig.	η_p^2	effect size f	d
Virtual neighbourhood						
Mean correct response (5 trials)	2	69.905	0.000**	0.710	0.791	1.938[a]
Mean response time (Sec)	2	94.324	0.000**	0.768	0.823	2.015[a]
Virtual maze						
Mean correct response (5 trials)	2	5.623	0.006**	0.165	0.402	0.557[b]
Mean response time (Sec)	2	13.210	0.000**	0.317	0.985	1.364[a]

** $p < 0.01$.
[a] Large Effect.
[b] Intermediate Effect.

more impairment in the number of correct responses and time of completion of trials in the virtual maze ($p < 0.05$). The comparison of patients with schizoaffective disorder and schizophrenia subjects indicated that there was no significant difference between the two groups ($p > 0.05$). The comparison of the schizoaffective disorder and control groups showed a significant difference only in response time ($p < 0.05$), but not in the number of correct responses in the virtual maze task (Table 3). The ANOVA results and effect size are presented in Table 4.

4. Discussion

This study explored allocentric and egocentric navigation deficits in patients with schizophrenia and schizoaffective disorder using virtual reality navigation tasks (VRNT). Today, virtual reality techniques are considered as useful tools for measuring allocentric and egocentric navigation deficits. In this study, a novel virtual reality environment we used to compare the visuospatial navigation deficits of the participants in two virtual environments (the virtual neighbourhood and the virtual maze). To the best of our knowledge, no studies have compared visuospatial memory statuses in schizoaffective disorder and schizophrenia patients using a virtual reality environment. We recently showed that schizophrenia patients were significantly impaired on all allocentric, egocentric, visual, and verbal memories tasks compared with bipolar patients, while there were no significant differences between bipolar and normal subjects (Mohammadi et al.,2018a).

In line with our previous report, patients with schizophrenia had the worst performances in all neuropsychological and navigational abilities compared with patients with schizoaffective disorder and control subjects. These findings suggest that schizophrenia and schizoaffective disorder patients performed worse on the RAVLT, ROCFT, and VRNT than schizoaffective disorder and control subjects, respectively. Overall, the schizoaffective subjects performed better than schizophrenia patients. They showed almost same pattern as schizophrenia patients in their performances on RAVLT, ROCFT, and VRNT, whereas their scores were significantly lower than those of control subjects in all these abilities. Conversely, no difference between normal individuals and bipolar patients was seen in our previous report (Mohammadi et al.,2018a). Therefore, it is suggested that allocentric and egocentric navigation deficits could be used as suitable features to determine cognitive impairments and as a differential diagnosis tool in patients with schizophrenia or schizoaffective disorder.

It is suggested that most psychotic disorders are not considered as distinct entities (Esterberg and Compton, 2009; Peralta and Cuesta, 2008). However, it has been suggested that schizoaffective disorder is a diagnostic entity which is distinguishable from both schizophrenia and affective psychoses (Kendler et al., 1995). Cognitive function may be one of the diagnostic characteristics to differentiate schizophrenia from schizoaffective disorder. Some investigations have explored cognitive functions in patients with schizoaffective disorder. Most previous studies have indicated cognitive deficits in patients with schizoaffective disorder compared with normal subjects and affective disorders (Bilder et al., 2000; Evans et al., 1999; Torrent et al., 2007; Van Rheenen et al., 2016). Often, there are considerable cognitive impairments in patients with schizophrenia (Dickinson et al., 2007). Comparisons of cognitive functions in patients with schizoaffective disorder and schizophrenia have showed controversial results. While some reports have noted no significant differences between patients with schizoaffective disorder and schizophrenia (which may be due to the small sample size of a study) (Bilder et al., 2000; Evans et al., 1999; Hanlon et al., 2006), others have observed certain differences in verbal and spatial working memory (Gruber et al., 2006; Reichenberg et al., 2009; Szoke et al., 2008; Torniainen et al., 2012).

Heretofore, no studies have directly compared allocentric and egocentric memories in schizoaffective disorder patients with schizophrenia using virtual reality techniques. Therefore, this study expanded the literature by suggesting that patients with schizoaffective disorder, like those with schizophrenia, show deficits in both allocentric and egocentric memories. However, the patients with schizoaffective disorder performed better in egocentric memory than those with schizophrenia, as they had fewer errors in the virtual maze. Previous studies have indicated that allocentric memory impaired and egocentric memory intact in patients with recent-onset schizophrenia (Agarwal et al., 2015; Folley et al., 2010; Landgraf et al., 2010; Siemerkus et al., 2012; Simonsen et al., 2011; Weniger and Irle, 2008; Wilkins et al., 2013). Moreover, the findings revealed that patients with schizoaffective disorder showed a similar pattern of impairment to that of schizophrenia, and they had more difficulties in allocentric navigation than in egocentric navigation. Compared to the normal subjects, patients with schizoaffective disorder and those with schizophrenia were impaired in the virtual tasks. The schizophrenia patients showed the severest impairment in visuospatial navigation tasks among all groups. Although patients with schizoaffective disorder performed better than those with schizophrenia, they performed significantly worse than the

Table 5
Spatial disorientation and visual/verbal memories deficits in schizophrenia and schizoaffective disorders.

Patients	Allocentric Differences	Main characteristics	Egocentric Differences	Main characteristics	Verbal memory	Visual memory
Schizophrenia	Impaired[a,e]	Getting lost and confused in navigation Longest response time among all groups	Impaired[a]	Better performance than allocentric Confused in navigation	Impaired[a,e]	Impaired[a,e]
Schizoaffective disorder	Impaired[a,c] Milder than schizophrenia	Getting lost and confused in navigation Better than schizophrenia	Not impaired[b,d] (in correct response) Like schizophrenia[a,d] (in response time)	Better performance than allocentric Little confused in navigation	Almost impaired[a,c]	Almost impaired[a,c]

a Significantly lower than normal subjects.
b Slightly lower than normal subjects, but not significant.
c Significantly better than schizophrenia.
d Slightly better than schizophreniapatients, but not significant.
e Significantly lower than schizoaffective subjects.

normal group. In addition, it was found that patients with schizoaffective disorder had milder impairments in visual, verbal, allocentric, and egocentric memories than patients with schizophrenia (Table 5).

Both the schizoaffective disorder group and the schizophrenia group had significantly worse performances in finding the given goal (the parking space) in the virtual neighbourhood task than the normal subjects. Exploring the time spent to reach the given goal indicated that schizophrenia and schizoaffective disorder patients required more time than schizoaffective disorder patients and normal subjects in the virtual neighbourhood, respectively. Comparing the performance of the participants in finding the given goal (the ball) in the virtual maze showed that schizoaffective disorder patients performed slightly better than schizophrenia subjects, but the difference was not significant. Compared with the normal subjects, however, a significant difference between the schizoaffective disorder patients and normal subjects was observed only in the time spent, but not in correct responses. As with the virtual neighbourhood task, patients with schizophrenia spent more time to find the given goal in the virtual maze than the other groups. Although patients with schizoaffective disorder completed the virtual task in less time than the schizophrenia patients, there was no significant difference between the two groups.

While some studies have reported that the executive function, processing speed, verbal, and nonverbal memories, are more intact in patients with schizoaffective disorder than those with schizophrenia (Fiszdon et al., 2007; Szoke et al., 2008), others have stated that patients with schizoaffective disorder performed significantly better than those with schizophrenia (Heinrichs et al., 2008; Szoke et al., 2008). A meta-analysis on cognitive functions indicated that the between-group differences of these patients were small (Boraet al., 2009). Overall, contrary to the differences in the severity of impairment, it was found that patients with schizophrenia showed a similar pattern of cognitive impairments to those with psychotic affective disorders (Reichenberg et al., 2009).

The use of neuroimaging technologies has provided a progression in the identification of disease-specific variations in brain structures and functions related to patients with schizophrenia and bipolar disorder, but there is little evidence related to patients with schizoaffective disorder as a distinct entity (Malhi et al., 2008). Compared with patients with bipolar disease and healthy subjects, the exploration of neuroanatomical structures in patients with schizoaffective disorder indicated that these patients display abnormalities in the striatal regions that were similar to those observed in patients with bipolar disorder (Getz et al., 2002). It has been supposed that patients with hippocampal impairments cannot complete spatial navigational tasks (Bohbot et al., 1998). Also, patients with temporal lobe injury are impaired in place learning or finding the path in a locomotor environment (Abrahams et al., 1997; Bohbot et al., 1998; Habib and Sirigu, 1987; Maguire et al., 1997). While striatal and parietal regions are involved in egocentric navigation, the medial structures of the temporal lobe and hippocampus have important roles in allocentric representations (Burgess et al., 2001; Etchamendy and Bohbot, 2007). Therefore, injury to these brain areas may be related to a rise in neuropsychiatric symptoms (Frith, 2005; Frith et al., 2000; Torrey, 2007).

Lesion studies in humans and animals (Ekstrom et al., 2003; Maguire et al., 1997; O'Keefe and Nadel, 1979; Rolls, 1999; Rolls and Xiang, 2006) and functional imaging studies in humans (Aguirre et al., 1996; Aguirre and D'Esposito, 1997; Barry et al., 2006; Bohbot et al., 2007, 2004; Burgess et al., 2001; Epstein et al., 2003; Etchamendy et al.,2012; Holdstock et al., 2000; Iaria et al., 2003; King et al., 2002; Maguire et al., 1997; Siemerkus et al., 2012) have suggested that allocentric navigation is dependent upon the hippocampal and parahippocampal cortices. Weinberger's group showed that an abnormal cortical response was observed in the DLPFC of patients with schizophrenia while performing spatial working memory tasks. The significant correlation was observed between DLPFC fMRI activation and working memory performance and supported the hypothesis that irregular PFC responses arose from abnormal PFC neurons (Callicott et al., 2000). Consistent with the results of Callicott et al. (2000)and Salgado-Pineda et al.(2016), it seems that the defect in spatial navigation in patients with schizoaffective disorder and schizophrenia is likely to be due to damage to DLPFC.

This is the first study to directly compare the allocentric and egocentric memories in patients with schizoaffective disorder and schizophrenia in a virtual neighbourhood with lots of navigational landmarks and in a virtual maze with no topographical landmarks. Contrary to previous findings that have suggested that egocentric memory remains intact in patients with recent-onset schizophrenia (Agarwal et al., 2015; Siemerkus et al., 2012; Weniger and Irle, 2008), the current results revealed that the performance of patients with schizophrenia in the virtual maze was significantly worse than that of normal subjects, and it was similar to that of schizoaffective disorder patients. Obviously, this potential differences in the cognitive/navigation abilities of chronic patients versus those with recent illness onset may be due to the disease stage. However, the patients with schizoaffective disorder performed better in egocentric memory than those with schizophrenia, as they had fewer errors in the virtual maze.

5. Conclusion

Taken together, the results led to the conclusion that allocentric memory is more impaired than egocentric in both schizoaffective disorder and schizophrenia patients, whereas patients with schizoaffective disorder performed better in egocentric memory than patients with schizophrenia (Table 5). It is further concluded that allocentric memory deficits can help differentiate patients with schizophrenia and schizoaffective disorder from healthy participants, whereas egocentric memory deficits can be used to distinguish them from each other. Given the similarity of cognitive impairments in patients with schizoaffective disorder or schizophrenia, it may be considered that the assessment, treatment, and rehabilitation of these patients could be administered in the same way. There is a continuing debate regarding the relationship between schizophrenia and schizoaffective disorder. The current findings suggest that schizophrenia and schizoaffective disorder share similar patterns of spatial navigational deficits, but patients with schizophrenia are more impaired than schizoaffective disorder subjects. It remains unclear whether schizoaffective disorder could be a diagnostic entity or a hybrid condition between schizophrenia and affective disorder. Further neuroimaging investigations are necessary to determine the neural damages associated with cognitive impairments in schizoaffective disorder. The main limitation of the present study was the unwillingness of patients to simultaneously perform the VRNT, RAVLT, and ROCFT with functional magnetic resonance imaging (fMRI), as the second phase of the project.

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