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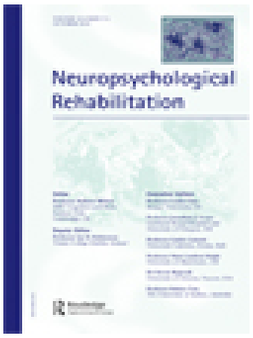

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Detecting allocentric and egocentric navigation deficits in patients with schizophrenia and bipolar disorder using virtual reality

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ABSTRACT

Present evidence suggests that the use of virtual reality has great advantages in evaluating visuospatial navigation and memory for the diagnosis of psychiatric or other neurological disorders. There are a few virtual reality studies on allocentric and egocentric memories in schizophrenia, but studies on both memories in bipolar disorder are lacking. The objective of this study was to compare the performance of allocentric and egocentric memories in patients with schizophrenia and bipolar disorder. For this resolve, an advanced virtual reality navigation task (VRNT) was presented to distinguish the navigational performances of these patients. Twenty subjects with schizophrenia and 20 bipolar disorder patients were compared with 20 healthy-matched controls on the newly developed VRNT consisting of a virtual neighbourhood (allocentric memory) and a virtual maze (egocentric memory). The results demonstrated that schizophrenia patients were significantly impaired on all allocentric, egocentric, visual, and verbal memory tasks compared with patients with bipolar disorder and normal subjects. Dissimilarly, the performance of patients with bipolar disorder was slightly lower than that of control subjects in all these abilities, but no significant differences were observed. It was concluded that allocentric and egocentric navigation deficits are detectable in patients with schizophrenia and bipolar disorder using VRNT, and this task along with RAVLT and ROCFT can be used as a valid clinical tool for distinguishing these patients from normal subjects.

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KEYWORDS Schizophrenia; Cognitive impairments; Allocentric; Egocentric; Virtual reality

Introduction

Schizophrenia is a complex neurobiological disorder, characterised by delusions, hallucinations, disorganised behaviours, and progressive cognitive impairments (Keshavan, Tandon, Boutros, & Nasrallah, 2008; Noori-Daloii et al., 2015; Van Os & Kapur, 2009). This disorder affects approximately 1% of the world population and has major effects on an individual's quality of life, including one's cognitive, social and occupational

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abilities (Green, 1996; Van Os & Kapur, 2009). Even though schizophrenia is a common and important psychiatric disorder, its particular neurophysiological basis is unknown (Strakowski, Delbello, & Adler, 2005). There is general consensus that schizophrenia is a neurodevelopmental disorder resulting from the interaction between multiple genetic susceptibilities and environmental risk factors (Andreasen, 2000, 2010; Piper et al., 2012). Neurodevelopmental variations in the glutamatergic system in the brain may have an important role in the progression of the illness (Kantrowitz & Javitt, 2012). Likewise, bipolar disorder or manic-depressive illness is a mental disorder which is characterised by episodes of mania, hypomania, and depression. According to the Global Burden of Disease Study 2015 (GBD 2015), the prevalence rates of schizophrenia and bipolar disorder have diminished compared to 2005. Even so, a high percentage of people still suffer from these diseases, such that they have become known as the 12th and 21st causes of disability worldwide, respectively (Kassebaum et al., 2016; Vos et al., 2016; Wang et al., 2016). Although current categorisation defines schizophrenia and bipolar disorder as a unique construct with different clinical features and probably distinct etiologies, there is sufficient evidence from neurobiological and molecular studies to indicate that these syndromes might share common susceptible genes which have significant associations with both illnesses (Cardno, Rijsdijk, Sham, Murray, & McGuffin, 2002; Moskvina et al., 2009). It has been shown that relatives of probands with bipolar disorder or schizophrenia are at increased risk of recurrent unipolar and schizoaffective disorders, suggesting an overlap in genetic liability (Cardno et al., 2002; Strakowski et al., 2005; Erlenmeyer-Kimling et al., 1997; Kendler, Gruenberg, & Tsuang, 1985).

A deficit in working memory, a set of processes for temporal storing, and the manipulation of information on a moment-to-moment basis may be the main causes of cognitive failure observed in schizophrenia (Goldman-Rakic, 1995). It is well established that patients with schizophrenia show an obvious impairment in verbal and spatial working memories (Fleming, Goldberg, Gold, & Weinberger, 1995; Kim, Glahn, Nuechterlein, & Cannon, 2004; Park & Holzman, 1992). These cognitive impairments have a great impact on daily functions and may be associated with poorer clinical output (Green, 1996). Present evidence suggests that decreased cognitive function may occur completely at the advanced clinical stage of the illness (Caspi et al., 2003; Eastvold, Heaton, & Cadenhead, 2007). Cognitive impairment is presented in the prodromal, psychotic, and chronic phases of schizophrenia (Fioravanti, Bianchi, & Cinti, 2012; Hill, Schuepbach, Herbener, Keshavan, & Sweeney, 2004; Mesholam-Gately, Giuliano, Goff, Faraone, & Seidman, 2009; Rund et al., 2004) and is observed in the first episode of the disease, generally in verbal memory, executive function, and attention (Addington & Addington, 2002; Townsend, Malla, & Norman, 2001). Despite progressive deterioration, cognitive deficits stabilise over time and play a central role in determining the course of the disease and its outcome (Rund et al., 2007; Townsend & Norman, 2004). Cognitive functions, such as verbal memory, and executive function are related to communication functions, while consciousness is related to social problem-solving abilities. These deficiencies could impair general function or functional outcome such as job and group performance, social skills, or problem-solving (Mueser, 2000).

For a long time, it has been thought that cognitive impairment in bipolar disorder is mainly secondary to acute mood symptomatology (Griffin, Pickar, & Kleinman, 1993). There is plenty of evidence to show that patients with bipolar disorder have numerous problems in working memory during different states of their illness. They may also have difficulties with tasks requiring retrieving and encoding online information (El-Badri,

Ashton, Moore, Marsh, & Ferrier, 2001; Krabhendam & Honig, 2000; Martínez-Arán et al., 2004; Rubinsztein, Michael, Paykel, & Sahakian, 2000). Regardless of clinical states, it seems that short-term storage of verbal information in bipolar disorder patients remains intact. While some reports have indicated that patients with bipolar disorder are intact in delayed spatial matching in trial samples (Gooding & Tallent, 2001; Park & Holzman, 1992; Park & Holzman, 1993), others have observed impairments in spatial maintenance, especially in the manic phase of the illness (McGrath, Chapple, & Wright, 2001; Sweeney, Kmiec, & Kupfer, 2000). Contrary to previous findings (Ferrier, Stanton, Kelly, & Scott, 1999; Gooding & Tallent, 2001; Park, 1997; Park & Holzman, 1992, 1993), McGrath et al. (2001) reported that patients with bipolar disorder showed significant impairment in spatial working memory tasks (McGrath et al., 2001). It has long been noted that schizophrenia and bipolar disorder may be distinctly similar to each other and may have an overlap in psychotic symptoms (Merikangas et al., 2002; Potash et al., 2001). Seidman et al. (2002) reported that because bipolar patients with mania display the same premorbid impairment as schizophrenic patients, these patients could be a precise comparison group for examining the diagnostic features of cognitive dysfunctions in schizophrenia (Seidman et al., 2002).

One of the most important findings in schizophrenia is abnormal hippocampal structure (Weiss, Dewitt, Goff, Ditman, & Heckers, 2005). Evidence from post-mortem examinations and patient brain imaging has demonstrated decreased volume and the presence of an abnormality in the shape of the hippocampus (Bogerts et al., 1990; Nelson, Saykin, Flashman, & Riordan, 1998; Shenton, Gerig, Mccarley, Szekely, & Kikinis, 2002; Wright et al., 2000). Such neuroimaging findings have also been observed in individuals in the first episode or prodromal phase of schizophrenia (Shenton et al., 2002). Structural imaging studies have suggested that reduced hippocampal volume is extended through the frontal to posterior regions, and it is not restricted to a particular region of the hippocampus (Weiss et al., 2005). Studies have also shown differences in the morphology (size, organisation, and shape) of hippocampal neurons in schizophrenic patients (Arnold et al., 1995; Benes, Sorensen, & Bird, 1991; Shenton et al., 2002; Zaidel, Esiri, & Harrison, 1997). It has been commonly accepted that the hippocampus is involved in episodic memory (Burgess, Maguire, & O'Keefe, 2002; Maguire & Frith, 2004), so it could be hypothesised that episodic memory impairment results from molecular and structural abnormalities in the hippocampus. Currently, it is widely accepted that the hippocampus plays an important role in spatial navigation tasks involving the construction of the cognitive map (Pigott & Milner, 1993). These tasks evaluate the capacity of binding events (for example, changing direction) with its spatial context (for example, the relation between landmarks). When the hippocampus is selectively injured, the person shows severe spatial memory impairment (Bohbot et al., 1998).

Neuroimaging studies have proved that the hippocampus, striatum (or caudate nucleus), and parahippocampal, posterior parietal, and medial prefrontal cortices are involved in visuospatial navigation (Burgess et al., 2002; Iaria, Petrides, Dagher, Pike, & Bohbot, 2003; Kumaran & Maguire, 2005; Shelton & Gabrieli, 2002). Interestingly, the visuospatial abilities have an intriguing interaction with a number of measures related to the pathogenesis of schizophrenia, such as empathy, schizotypy, and theory of mind (Bosia, Riccaboni, & Poletti, 2012; Decety & Lamm, 2007; Iacoboni & Dapretto, 2006; Thakkar & Park, 2010). Currently, spatial navigation and memory have been modelled and supported by allocentric representations (world-centered) which

are independent of the observer, and egocentric representations (body-centered) which are related to the axes of the body. The models of visuospatial abilities suggested two visual space perspectives: allocentric reference (object- or environment-centered) and egocentric reference (ego- or body-centered) (O'Keefe & Nadel, 1979). While egocentrism refers to the ability to see the world from a personal view, allocentrism refers to the capacity of experiencing the world from an identical and more impersonal view. Egocentric referencing has a pivotal role in keeping a constant moment-to-moment perception, while allocentric referencing is encouraged through more understanding of the environment (Barry et al., 2006).

It has been revealed that the hippocampus and medial structures of the temporal lobe are involved in allocentric representations, while the striatal and parietal regions have an important role in egocentric processing (Burgess, Maguire, Spiers, & O'Keefe, 2001; Etchamendy & Bohbot, 2007). In addition, Zhang and Ekstrom (2013) demonstrated that interactions of the hippocampus with the posterior-superior parietal cortex are key in allocentric representation (Zhang & Ekstrom, 2013). Hence, damage to these brain regions may be associated with the emergence of neuropsychiatric symptoms (Frith, 2005; Frith, Blakemore, & Wolpert, 2000; Torrey, 2007).

It has been previously reported that patients with impairments at the hippocampus level cannot complete spatial tasks (Bohbot et al., 1998). It has been proposed that the allocentric representation of spatial context is dependent on the ventromedial-temporal declarative memory organisation. It is revealed that patients with temporal lobe damage are impaired in place learning or finding the track in a locomotor environment (Abrahams, Pickering, Polkey, & Morris, 1997; Bohbot et al., 1998; Habib & Sirigu, 1987; Maguire, Burke, Phillips, & Staunton, 1996). It is believed that striatum, medial, and posterior parietal cortices encode egocentric synchronisations (Aguirre & D'esposito, 1997; Burgess et al., 2001; Epstein, Graham, & Downing, 2003). In line with these reports, Zedkova, Woodward, Harding, Tibbo, and Purdon (2006) suggested that schizophrenic subjects show hypoactivation of frontoparietal cortices and caudate versus hyperactivation of other regions while performing the task (Zedkova et al., 2006).

Among the many aspects of cognitive functions which have been investigated in schizophrenia, spatial cognition is an interesting topic to study. Spatial cognition is associated with the acquisition, storage, and retrieval of information about spatial environments. This ability enables people to manage location, direction, and movement, and to govern where they are (orientation), how to get resources, and how to find their way. In contrast, spatial disorientation is the inability to properly regulate body position in an environment. Hence, it is important to assess spatial navigation to prevent these problems. So far, a few virtual reality studies have been conducted to investigate allocentric and egocentric navigation deficits in schizophrenia, but studies on both memories in bipolar disorder are lacking. Some studies have suggested that individuals with medial temporal lobe damage are basically impaired in allocentric and/or egocentric spatial learning (Abrahams et al., 1997; Aguirre & D'esposito, 1997; Epstein et al., 2003; Folley, Astur, Jagannathan, Calhoun, & Pearlson, 2010; Habib & Sirigu, 1987; Hanlon et al., 2006; Landgraf et al., 2010; Maguire et al., 1996; Packard, Hirsh, & White, 1989; Spiers et al., 2001; Weniger & Irle, 2008).

The development of virtual reality technologies has allowed great progress to be made in the study of spatial navigation and memory. The use of virtual reality, administered as a computer simulation of the first-person view of an environment that could simulate navigation in a large environment, has provided a great benefit to evaluating

spatial navigation and memory status. In the present study, the authors' newly-developed virtual reality navigation task (VRNT) with two virtual reality environments (virtual neighbourhood and virtual maze) were used to evaluate spatial navigation in allocentric and egocentric referencing. The purpose of this comparative study was to determine for the first time ever the allocentric and egocentric navigation deficits of and differences between patients with schizophrenia and bipolar disorder using virtual reality.

Methods

Participants

Sixty subjects (20 patients with schizophrenia, 20 patients with bipolar disorder, and 20 normal subjects) were recruited from outpatient services at Imam Hossein Hospital (Tehran, Iran). All subjects signed a standard informed consent form approved by the local ethics committee. Participants with schizophrenia and bipolar disorder were referred to the clinic by a psychiatrist. Cognitively normal subjects, who were recruited by public advertisement, reported no memory difficulties, and this was confirmed by neuropsychological assessment. In the psychiatry clinic, participants were evaluated by a psychiatrist who obtained a medical history from each patient and diagnosed patients based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria. Psychological procedures used for the diagnosis were presented in the Neuropsychological Department. Only subjects with no other neurological or psychiatric diseases were included in this study. The Ethical Committee of the Baqiyatallah University of Medical Sciences approved the study design.

Procedure

All participants underwent a neuropsychological assessment and visuospatial navigation tasks, including the Rey-Osterrieth complex figure test and the authors' newly-developed VRNT. The assessment was carried out within 6 months.

Neuropsychological assessment

A neuropsychological assessment was performed to cover the following cognitive series: (1) Verbal memory: Auditory-Verbal Learning Test (AVLT, sum of trials 1–5, recall after intervention, delayed recall after 30 min, and memory recognition) (Jafari, Steffen Moritz, Zandi, Aliakbari Kamrani, & Malyeri, 2010); (2) Non-verbal memory: Rey-Osterrieth Complex Figure Test (ROCFT-R; recall condition, immediate) (Meyers & Meyers, 1995); (3) Visuospatial memory: Rey-Osterrieth Complex Figure Test (ROCFT-D; after 30 min delay) (Meyers & Meyers, 1995); and (4) the Mini-Mental State Examination (MMSE) (Ansari, Naghdi, Hasson, Valizadeh, & Jalaie, 2010) performed to measure global cognitive function.

Virtual reality environment tasks

Test design

The virtual reality environment techniques were described previously (Weniger & Irle, 2006) and have been used to explore allocentric and egocentric memories (Weniger & Irle, 2008). The environments were three-dimensional, fully coloured, textured, and

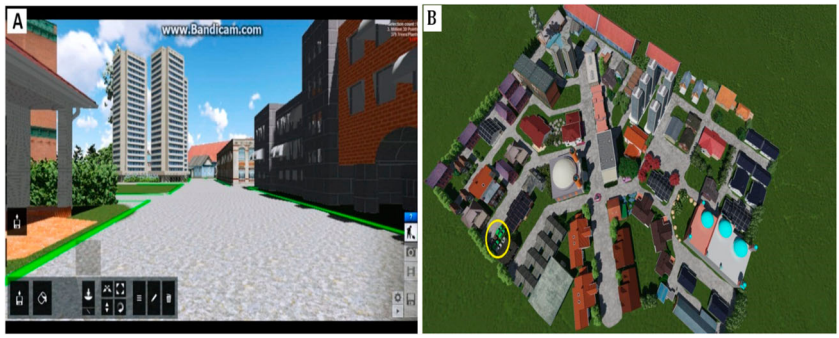

Figure 1. The first person view (A), and Overhead view (B) of virtual neighbourhood.

presented a first-person view. Movements in the environment could be controlled by subjects using a joystick. The authors' novel VRNT was designed with two virtual environments (virtual neighbourhood and virtual maze) to evaluate allocentric (virtual neighbourhood) and egocentric (virtual maze) spatial navigation. The virtual neighbourhood was designed to be similar to the real environment (real neighbourhood) (Figure 1).

The virtual neighbourhood contained relevant navigational landmarks to help subjects find the route, but there were no landmarks in the virtual maze; subjects had to find the goal by recalling their ways from memory (Figure 2).

In the VRNT, each environment (virtual neighbourhood and virtual maze) consisted of a 3D first-person view and a 2D overhead view of the environment. First, the 2D overhead view of the environment was presented to the subjects for 60 seconds (Figures 1B and 2B). Then a 3D first-person view was presented. Finally, subjects were asked to find the given goal [parking in the virtual neighbourhood (Figure 1A) and a ball in the virtual maze (Figure 2A)] which had been marked in a 2D overhead view (yellow circle). Each subject received three trials to be familiar with the tasks; then they were given five trials. The reactions and response times were then recorded.

The 3D first-person view images were created using AutoCAD, Adobe Photoshop CS6, and Autodesk 3ds Max software packs running within Lumion pro 5.0 editors. The sizes of the first-person view and the overhead view images were 1920×1080 px and 1280×720 px, respectively, and they were projected on a 15.6″ LCD monitor. Both versions of the test were offered, and the resulting files were processed to

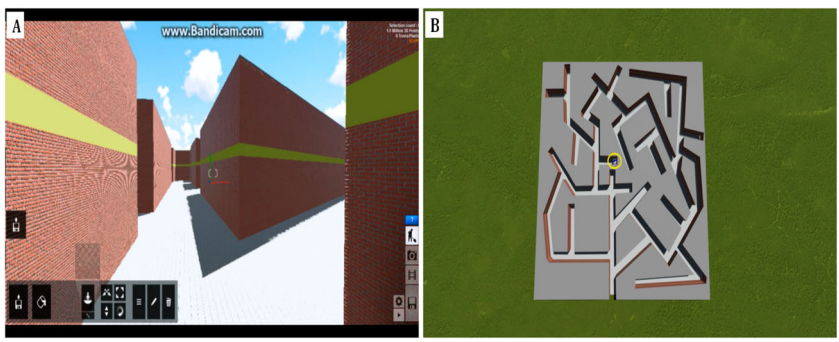

Figure 2. The first person view (A), and Overhead view (B) of virtual maze.

produce primary data tables for further statistical analyses. Depending on the viewpoint of the landmarks, the two analyzed measures from the test were the response time and the number of correct responses.

Scoring

Both the number of correct responses and the response time were computed for each of the five trials of the virtual neighbourhood and virtual maze in each version of the test; they were considered as dependent variables in statistical analyses.

Statistical analysis

Differences in demographic variables among groups were analyzed using one-way ANOVA tests and post-hoc Tukey HSD tests. Neuropsychological test scores and performance on the VRNT (correct responses and the time of response) were analyzed by one-way ANOVA tests. Correlation analysis was applied to measure the relationship between neuropsychological variables and each subject's performance on the VRNT. In all analyses, two-tailed .05 was considered an indication of a significant difference. Statistical analyses were carried out by SPSS v. 22.

Results

Descriptive statistics and neuropsychological scores

The groups did not differ in years of education (almost all participants were at the same level of education) and handedness ($p = .05$), but they differed in age ($p < .001$), MMSE scores ($p < .001$), and duration of the disorder ($p < .005$). The schizophrenia and bipolar disorder groups were predominantly female (60% and 65%, respectively), whereas the normal group had an equal number of men and women. Demographic characteristics of the participants are presented in Table 1.

Neuropsychological tests displayed significant between-group effects. In all tests, the schizophrenia group had lower scores in comparison with the normal and bipolar disorder groups ($p < .001$). Similarly, the bipolar disorder group had lower scores than the normal group in all tests, but the differences were not significant ($p > .05$). These findings confirm the fact that the classification of the groups was also based on the results of neuropsychological tests. See Table 2 for more details on the neuropsychological characteristics of the groups.

Virtual reality navigation task (virtual neighbourhood and virtual maze)

The scores of VRNT and response times of all participants were analyzed using the one-way ANOVA test. The analysis revealed significant differences between groups in the virtual neighbourhood ($p < .001$) and virtual maze ($p < .05$) tasks.

Virtual neighbourhood task

Comparing the scores of the schizophrenia, bipolar disorder, and control subjects across five trials of the virtual neighbourhood revealed significant differences among groups ($p < .001$). Statistical analysis showed that schizophrenia patients performed

Table 1. Demographic characteristics of the groups.

Characteristics	Normal controls ($n = 20$)	Participants with schizophrenia ($n = 20$)	Participants with bipolar disorder ($n = 20$)
Age (Year)	40.9 ± 5.784	42.45 ± 9.61**	31.15 ± 7.659*
MMSE	29.5 ± .888	27.45 ± 1.82†	29.4 ± 1.046††
Education (Year)	12.95 ± 1.877	12.7 ± 2.677	13.05 ± 1.637
Handedness (Right:Left)	18:2	18:2	18:2
Sex (Female:Male)	10:10	12:8	13:7
Duration of disorder (Year)	NA	12.2 ± 4.979	7.2 ± 5.671
First episode (Yes:No)	–	3:17	NA
Extrapyramidal motor symptoms[a] (None: Mild: Moderate: Severe)	–	20: 0: 0: 0	20: 0: 0: 0
DSM-IV subtype, (No)	–		
Schizophrenia:			
Paranoid		13	
Disorganised		6	
Undifferentiated		1	
Bipolar disorder:			
Type 1			9
Type 2			11

MMSE, total score; Handedness, based on Edinburgh Handedness Inventory; DSM-IV = 4th edition of the Diagnostic and Statistical Manual of Mental Disorders.

[a]Symptoms included: Akathisia, Wrist rigidity, Tremor, Abnormal involuntary movements, Tardive dyskinesia and Dystonia.

Values are mean ± SD.

*$p \leq .001$, statistical comparisons (ANOVA with post hoc Tukey HSD): to the normal group.

**$p < .001$, statistical comparisons (ANOVA with post hoc Tukey HSD): to the bipolar disorder group.

†$p < .001$, statistical comparisons (ANOVA with post hoc Tukey HSD): to the normal group.

††$p < .001$, statistical comparisons (ANOVA with post hoc Tukey HSD): to the schizophrenia group.

significantly lower than the normal group on the virtual neighbourhood task ($p < .001$). Similarly, bipolar disorder patients scored lower than the normal group, but the difference was not significant ($p > .05$). In addition, response time analysis indicated that schizophrenic subjects to longer times to complete trials than the bipolar disorder and control subjects ($p < .001$), but there was no significant difference between the bipolar disorder subjects and the control group ($p > .05$).

Virtual maze task

Comparisons revealed that schizophrenia patients performed significantly worse than the normal group in the virtual maze task ($p < .05$), but no significant difference was observed between the performance of patients with schizophrenia and those with bipolar disorder ($p > .05$). Moreover, the response time analysis indicated that schizophrenic subjects took longer time to complete trials than the control subjects ($p \leq .002$), but there was no significant difference between subjects with schizophrenia and those with bipolar disorder ($p > .05$) (Table 3).

Relationship between neuropsychological and virtual neighbourhood performance

To determine the relationship between neuropsychological assessment and performance of virtual neighbourhood task, Pearson's correlation coefficient was used. Correlation tests demonstrated a strong positive correlation between the scores of

Table 2. Neuropsychological characteristics of the groups.

Characteristics	Normal controls ($n = 20$)	Participants with schizophrenia ($n = 20$)	Participants with bipolar disorder ($n = 20$)
RAVLT			
Total score	49.15 ± 4.671	32.2 ± 5.671*	48.5 ± 5.642**
Immediate recall scores	10.54 ± 1.503	5.7 ± 1.75*	9.95 ± 1.82**
Delayed recall scores	9.85 ± 1.814	5.3 ± 1.417*	9.4 ± 2.233**
Memory recognition	13.4 ± 1.095	9.8 ± 1.5*	13.05 ± 1.394**
ROCFT			
Immediate recall scores	10.25 ± 1.118	7.85 ± 1.814†	9.65 ± 1.565††
Delayed recall scores	9.2 ± 1.151	6.8 ± 2.166†	8.7 ± 1.341††
SAPS/SANS: Positive symptoms	–	2.1 ± 1.3	–
SAPS/SANS: Negative symptoms	–	2.3 ± .9	–
SAPS/SANS: Disorganised symptoms	–	1.7 ± .8	–
SAPS	–	–	1.93 ± 1.76
HRSD	–	–	12.93 ± 8.79
BR Mania	–	–	16.2 ± 4.91
BPRS	–	–	33.17 ± 6.71

NA, not applicable; RAVLT, The Rey Auditory Verbal Learning Test; 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, Rey-Osterrieth complex figure test; ROCFT Immediate recall score, recall immediately; ROCFT Delayed recall score: recall after 30 min; SAPS, Scale for the Assessment of Positive Symptoms; SANS, Scale for the Assessment of Negative Symptoms; HRSD, Hamilton Rating Scale for Depression; BR Mania, Bech-Rafaelsen Mania Scale; BPRS, Brief Psychiatric Rating Scale.

Values are mean ± SD.

*$p < .001$, statistical comparisons (ANOVA with post hoc Tukey HSD): to the normal group.

**$p < .001$, statistical comparisons (ANOVA with post hoc Tukey HSD): to the schizophrenia group.

†$p < .001$, statistical comparisons (ANOVA with post hoc Tukey HSD): to the normal group.

††$p < .001$, statistical comparisons (ANOVA with post hoc Tukey HSD): to the schizophrenia group.

neuropsychological and virtual neighbourhood performances among all subjects ($p < .01$). There was a strongly negative correlation between neuropsychological scores and the mean response time in the virtual neighbourhood as well ($p < .01$) (Table 4).

Relationship between neuropsychological and virtual maze performance

Correlation tests demonstrated that there was a positive relationship among all neuropsychological and virtual maze scores ($p < .01$) except memory recognition scores which had a weaker correlation with virtual maze scores ($p < .05$). Also, measuring the

Table 3. The performance of groups on virtual reality (virtual neighbourhood, virtual maze) tasks.

Virtual reality task	Normal controls ($n = 20$)	Participants with schizophrenia ($n = 20$)	Participants with bipolar disorder ($n = 20$)
Virtual neighbourhood			
Mean correct response (5 trials)	4.9 ± .307	2.95 ± .604*	4.65 ± .67†
Mean response time (Sec)	53.24 ± 8.129	110.42 ± 15.552*	63.46 ± 19.942†
Virtual maze			
Mean correct response (5 trials)	4.6 ± .598	3.85 ± .745**	4.15 ± 1.268
Mean response time (Sec)	64.79 ± 16.441	93.62 ± 18.4††	79.28 ± 35.197

The 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

*$p < .001$, statistical comparisons (ANOVA with post hoc Tukey HSD): to the normal group.

**$p < .05$, statistical comparisons (ANOVA with post hoc Tukey HSD): to the normal group.

†$p < .001$, statistical comparisons (ANOVA with post hoc Tukey HSD): to the schizophrenia group.

††$p \leq .002$, statistical comparisons (ANOVA with post hoc Tukey HSD): to the normal group.

Table 4. Correlation between neuropsychological and virtual reality environments scores.

Test	Virtual neighbourhood	Mean response time of Virtual neighbourhood	Virtual Maze	Mean response time of Virtual Maze
RAVLT 1–5	.841**	−.816**	.361**	−.433**
RAVLT_Immediate	.776**	−.746**	.344**	−.421**
RAVLT_Delayed	.756**	−.727**	.335**	−.416**
Memory Recognition	.755**	−.731**	.279*	−.361**
ROCFT-Immediate	.621**	−.624**	.508**	−.556**
ROCFT-Delayed	.588**	−.585**	.405**	−.457**

RAVLT, The Rey Auditory Verbal Learning Test; RAVLT total scores, sum of trials 1–5; RAVLT immediate recall, recall after interference; RAVLT delayed, recall after 30 min; Memory recognition, total word remembered from presented words; ROCFT, Rey-Osterrieth complex figure test; ROCFT Immediate recall score, recall immediately; ROCFT Delayed recall score, recall after 30 min.
Values are mean ± SD.
*Correlation is significant at the .05 level (2-tailed).
**Correlation is significant at the .01 level (2-tailed).

relationship between neuropsychological scores and mean response time of a virtual maze revealed a negative correlation among all participants ($p < .01$) (Table 4).

Discussion and conclusion

The goal of this study was to compare the allocentric and egocentric memories in patients with schizophrenia, bipolar disorder, and normal subjects. There was no significant difference in age between the participants with schizophrenia and the normal control, but there were significant age differences between the bipolar disorder and control groups and between the bipolar disorder and schizophrenia subjects as well. In contrast to the normal group, the total MMSE scores of schizophrenia subjects were significantly lower than those of control subjects, but there was no significant difference between those of subjects with bipolar disorder and control subjects. Moreover, the bipolar group had better MMSE scores than the schizophrenia patients. To the best of our knowledge, this is the first comparative study which investigated allocentric and egocentric memories among these patients through virtual reality. A previous study showed that virtual reality environments could be used as a suitable tool for measuring spatial navigation and memory performance in schizophrenia patients. The authors suggest that virtual realities provide a major benefit for the assessment of visuospatial memory ability, since computer-based first-person simulation environments can simulate spatial navigation in a large-scale space (Weniger & Irle, 2008).

For this purpose, we designed a new task of virtual reality in the two environments of neighbourhood and maze, derived from previously described techniques (Weniger & Irle, 2006). Two versions of VRNT (virtual neighbourhood and virtual maze) were compared in patients with schizophrenia, bipolar disorder, and control subjects. In agreement with previous studies which have reported allocentric memory impairment, intact egocentric memory in recent-onset schizophrenia patients (Agarwal et al., 2015; Folley et al., 2010; Siemerkus, Irle, Schmidt-Samoa, Dechent, & Weniger, 2012; Weniger & Irle, 2008; Wilkins et al., 2013), and working memory impairment in bipolar disorder patients (McGrath et al., 2001; Zhang et al., 2012), we hypothesised that patients with schizophrenia might be impaired in the virtual neighbouhood and maze more than the bipolar disorder and control subjects.

This assumption was supported, as the current results revealed, by the fact that schizophrenia patients were impaired in the virtual neighbourhood and performed

lower than the bipolar disorder and control subjects with regard to both correct responses and reaction times. The findings revealed a greater impairment in patients with schizophrenia in finding their route in the virtual neighbourhood, including losing relevant guidance landmarks and taking a long time to reach the goal (to find the parking spot in the virtual neighbourhood); they performed significantly lower than both bipolar disorder and control subjects, but no significant differences were seen between bipolar disorder and control subjects. The impaired performance of the allocentric memory of schizophrenia patients in the Morris water task cannot be described by impaired navigational capabilities (Hanlon et al., 2006). Similarly, the deficits of the allocentric memory of the schizophrenia patients in the current study cannot be explained by deficits in navigational capabilities, as their performance in the virtual maze was a little lower than the bipolar disorder and control subjects. Although no investigation exploring allocentric and egocentric memories in bipolar disorder patients using virtual reality environment was found in the literature search, several studies have reported that spatial working memory is impaired in these patients (Badcock, Michie, & Rock, 2005; Barrett, Kelly, Bell, & King, 2008; Gould et al., 2007; McGrath et al., 2001; Pirkola et al., 2005; Sweeney et al., 2000; Zhang et al., 2012).

It may be considered that the use and storage of navigational landmarks (which are impaired in schizophrenic subjects) depend on a ventromedial-temporal declarative memory structure. It has long been known that schizophrenic subjects display a noticeable reduction in hippocampal volume (Geuze, Vermetten, & Bremner, 2005; Honea, Crow, Passingham, & Mackay, 2005; Wright et al., 2000). Functional neuroimaging studies (Aguirre & D'esposito, 1997; Bohbot, Iaria, & Petrides, 2004; Burgess et al., 2001; Epstein et al., 2003; Iaria et al., 2003; Siemerkus et al., 2012) as well as single unit recordings and lesion studies (Ekstrom et al., 2003; Maguire et al., 1996; O'Keefe & Nadel, 1979; Rolls, 1999; Rolls & Xiang, 2006) have indicated that allocentric capabilities depend on hippocampal and parahippocampal cortices. In this context, it is widely accepted that the hippocampus has an important role in spatial navigation (Pigott & Milner, 1993); so, damage to the hippocampus and the posterior-superior parietal cortex may be associated with a rise in neuropsychiatric symptoms (Frith, 2005; Frith et al., 2000; Torrey, 2007). In addition, interactions between these brain regions play a crucial role in allocentric representation (Zhang & Ekstrom, 2013). On the other hand, patients with impairments at the hippocampus level cannot complete spatial tasks (Bohbot et al., 1998). Likewise, the hippocampus and medial structures of the temporal lobe are involved in allocentric representations, while the striatal and parietal regions are important in egocentric processing (Burgess et al., 2001; Etchamendy & Bohbot, 2007). Based on the observed better performance of egocentric memory than that of allocentric in both schizophrenia and bipolar disorder patients, it can be concluded that they may have more problems in the hippocampus, posterior-superior parietal cortex, and medial structures of the temporal lobe than in the striatal and parietal regions. The current findings testify to the fact that these patients probably have more problems in the hippocampus, posterior-superior parietal cortex, and medial structures of the temporal lobe as shown in previous studies (Abrahams et al., 1997; Bohbot et al., 1998; Habib & Sirigu, 1987; Hanlon et al., 2006; Landgraf et al., 2010; Maguire et al., 1996; Spiers et al., 2001; Weniger & Irle, 2008).

The present study is the first to explore the egocentric navigation and memory storage of schizophrenic subjects in comparison with bipolar disorder and control subjects in a virtual maze with no topographical landmarks. Unlike previous investigations

which have suggested that the egocentric memory of schizophrenia patients was entirely normal (Agarwal et al., 2015; Siemerkus et al., 2012; Weniger & Irle, 2008), this study found that in the virtual neighbourhood, the performance of schizophrenic subjects was significantly lower than that of bipolar and normal subjects. In addition, the results showed that bipolar disorder patients performed lower than control subjects, but there were no significant differences between these two groups.

Measuring the time required to reach the goal in the virtual maze (to find the ball) among bipolar disorder and control subjects showed that completing each trial took a longer time in the virtual maze than in the virtual neighbourhood. Nevertheless, schizophrenic subjects recorded longer response times than other groups, because they made a large number of errors in the virtual neighbourhood. This finding is even more surprising, as bipolar disorder patients and control subjects had more difficulties in finding their ways in the virtual neighbourhood compared with the virtual maze, while schizophrenia patients performed better in the virtual maze than in the virtual neighbourhood. Some previous studies have demonstrated that schizophrenia and bipolar disorder patients and their unaffected relatives show spatial working memory impairments (Cannon et al., 2000; Fleming et al., 1997; Park & Holzman, 1992; Pirkola et al., 2005), but others have reported that patients with bipolar disorder are not impaired in a spatial working memory task in the euthymic phase of illness (Clark, Iversen, & Goodwin, 2002; Ferrier et al., 1999; Gooding & Tallent, 2001; Kieseppä et al., 1999; Pirkola et al., 2005). McGrath et al. (2001) indicated that patients with schizophrenia and mania are impaired in spatial working memory (McGrath et al., 2001). Due to these opposing reports and the importance of the clinical state of bipolar patients and to better understand bipolar disorder pathogenesis, we proposed that allocentric and egocentric memories scores in bipolar patients did not differ significantly from the scores of normal subjects. In contrast, both allocentric and egocentric memories were impaired in patients with schizophrenia.

The negative correlation between neuropsychological scores and mean response times in the virtual neighbourhood and virtual maze in this study demonstrates that the deficit may be mediated in part by negative symptoms. This is in line with previous reports of a correlation between allocentric memory performance and intensity of negative symptoms (Agarwal et al., 2015; Folley et al., 2010).

With all results taken together, it was concluded that schizophrenia patients were impaired on all allocentric, egocentric, visual, and verbal memory tasks compared with bipolar disorder patients and normal subjects; albeit, their egocentric memory was better than their allocentric memory; they got lost and confused in navigation (Table 5).

Table 5. Comparative spatial navigation and visual/verbal memory deficits in schizophrenia and bipolar disorder.

Patients	Allocentric	Egocentric	Verbal memory	Visual memory
Schizophrenia	Impaired[a] (Getting lost and confused in navigation)	Impaired[a] (Better performance than allocentric, Longer response time than allocentric and confused in navigation)	Impaired[a]	Impaired[a]
Bipolar disorder	Almost not impaired[b] (Little confused in navigation)	Almost not impaired[b] (Better performance than allocentric and longer response time than allocentric)	Almost not impaired[b]	Almost not impaired[b]

[a]Significantly lower than normal subjects.
[b]Slightly lower than normal subjects, but not significant.

Although the bipolar disorder patients were not impaired in these abilities, they performed better in egocentric memory tasks than allocentric memory tasks, and their visual and verbal memories were insignificantly lower than normal subjects (Table 5).

In conclusion, the current study revealed significant differences between the performances of schizophrenia, bipolar disorder, and control subjects in a virtual reality task and suggested that virtual neighbourhood and virtual maze tasks can be valid neuropsychological markers for distinguishing schizophrenia patients from bipolar disorder and control subjects. The distinction between two forms of visuospatial memories would be more valuable with further investigation using concurrent neuroimaging studies. Further research should be conducted to investigate allocentric and egocentric abilities in other neuropsychiatric disorders to determine whether this cognitive ability can be used to distinguish between diseases with similar clinical presentations.

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