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Original Article

Neurocognitive Functions Related to Parietal Lobe in Patients with Schizophrenia and Methamphetamine Induced Psychotic Disorder and Healthy Individuals: A Comparative Study

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Abstract

Background: There are some inconsistent findings about neurocognitive functions in schizophrenia and methamphetamine induced psychosis (MIP). This study aimed to compare these two disorders in terms of neurocognitive functions related to parietal lobe.

Methods: This was a cross-sectional study in which 30 patients with schizophrenia, 30 patients with MIP, and 32 healthy individuals were compared. The two groups of patients were selected through convenience sampling from among patients hospitalized in Shahid Beheshti hospital in Kerman, Iran and healthy individuals were selected via convenience sampling from among the employees of Kerman University of Medical Sciences. The three groups were administered clock-drawing test (CDT), Rey-Osterrieth complex figure (ROCF) copying test, and interlocking finger test (IFT) and their demographic and clinical data were collected. The one-way analysis of variance (ANOVA) was used to investigate the differences between the groups. Multivariate analysis of covariance was also used to examine the effects of confounding factors. Besides, follow-up pairwise comparisons were performed after adjustment for multiple testing.

Findings: The group with schizophrenia had significantly more impairment than the group with MIP with reference to the results of IFT and the ROCF test. However, the scores of patients with MIP on these two tests were not different from those of the normal controls. With regard to the CDT, the only significant difference was observed between the group with schizophrenia and controls.

Conclusion: On the condition that the results are replicated in other studies, some parietal lobe neurocognitive tests might be used when it is difficult to differentially diagnose schizophrenia and MIP.

Keywords: Schizophrenia, Methamphetamine, Neurocognitive tests, Parietal lobe

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Introduction

Research has shown that methamphetamine induced psychosis (MIP) has just now turned into a major health problem.[1,2] Recreational methamphetamine users have been estimated to be two or three times more likely to show psychotic symptoms than the general population. Moreover, regular methamphetamine users reveal psychotic symptoms 11 times more than the general population.[3]

Given the emphasis on dopamine neurotransmission in schizophrenia, MIP has long been regarded as a model for schizophrenia. Correspondingly, neurocognitive studies have sought to compare these two disorders, and there is inconsistency in the results of the studies.[4] Jacobs et al found no significant difference between patients hospitalized with MIP and those with paranoid schizophrenia in eight cognitive domains of premorbid intellectual ability, learning and memory, executive functioning, general intellectual functioning, attention and concentration, motor abilities, and non-verbal and verbal skills.[4] Ezzatpanah et al also reported that two groups of patients with schizophrenia and MIP performed similarly in the domains of executive functioning, selective attention, sustained attention, and memory; however, the group suffering from schizophrenia underperformed MIP group in sustained visual attention as a domain related to the parietal lobe.[5] Besides, Khalkhali et al in a study on cognitive functions related to parietal lobe, showed better performance of the group with MIP than the patients affected with schizophrenia in terms of the right-side visual search and attention test (VSAT) results; on the contrary, they found no significant difference between these two

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groups concerning the left-side VSAT, total VSAT, and Rey-Osterrieth complex figure (ROCF) test results.[6]

Considering inconsistencies in the results of previous studies, the present study aimed to compare a group of patients with MIP, a group of schizophrenic patients, and a normal control group in terms of the visual-constructional domain of the parietal lobe neurocognitive tests including the ROCF, interlocking finger test (IFT), and clock-drawing test (CDT), which were associated with each other as confirmed in a study by Moo et al.[7]

Methods

Participants and procedure

This was a cross-sectional study comparing the three groups of patients with schizophrenia, patients with MIP, and healthy controls. With the alpha, beta, and ratio of variance to minimum detectable difference being estimated as 0.05, 0.8, and 2, respectively, the sample size was calculated to be 30 participants in each group. The documented diagnoses in the patients' hospital records made by board-certified psychiatrists and then confirmed by a fourth-year resident of psychiatry (NM) according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) were considered as the selection criteria of the patients with schizophrenia and MIP. Moreover, a positive urine test for methamphetamine use was needed for the patients with MIP to be included. Both groups of patients were selected through convenience sampling from among the inpatients at Shahid Beheshti Hospital, a referral center for psychiatric admission in the Southeast of Iran. All individuals with schizophrenia and MIP were under antipsychotic drug treatment. Assessments were further performed on the patients of these two groups after psychosis was stabilized, that is, the total score of the Positive and Negative Syndrome Scale (PANSS) and the score of each of the seven subscales of the PANSS positive symptoms had to be less than 70, and 3, respectively. An informed consent was also taken from all participants and their caregivers after giving information about the study process.

Both groups of patients were matched with each other and with the normal control group on their age, gender, and level of education. In other words, for each patient with schizophrenia, a counterpart with MIP and a normal individual with similar age, gender, and level of education were selected. Opioid use disorder in both groups of patients was also considered as a cofounding variable and then controlled through analysis. The normal control group consisted of 32 participants selected via convenience sampling from among the employees of Kerman University of Medical Sciences, Kerman, Iran.

The inclusion criteria for the participants were being 20-50 years old, having more than five years of formal education, suffering from no organic brain disease, and having no history of traumatic brain injury, physical anomaly, or visual disturbance. Furthermore, the participants with the history of psychotic symptoms before methamphetamine use in the group with MIP, the history of methamphetamine use disorder (MUD) in the group suffering from schizophrenia, and the history of psychiatric disorders or MUD in the normal control group were excluded. The patients with the history of electroconvulsive therapy during the last six months were also excluded. It is worth noting that the normal control participants had no history of major psychiatric disorders (i.e., anxiety, mood, or psychotic disorders), no history of psychiatric treatment, and no family history of psychosis.

Instruments

In addition to the demographic characteristics including age, gender, and level of education for all participants, the data about the concurrent use of benzodiazepine, anticonvulsant, and anticholinergic drugs and the comorbidity of opioid and cannabis use disorders were collected in both groups of patients. Moreover, the data about methamphetamine use duration and pattern were elicited from each patient in the group with MIP.

Positive and Negative Syndrome Scale

Upon its publication in 1987, the PANSS has been widely implemented in the assessment of psychotic symptoms to investigate the efficacy of antipsychotics. This test consists of a positive scale (7 items), a negative scale (7 items), and a general psychopathology scale (16 items), wherein each item is scored between one and seven and the total score of the PANSS ranges from 30 to 210.[8]

Clock-drawing test

The participants were asked to draw an analogue clock face from memory, write all the numbers on their own positions, and then set the clock by drawing the hands in a way that the clock indicated the time "ten after eleven". The scoring was made according to the scoring system described by Sunderland et al in 1989 and the test was scored on a scale of 1-10, depending on the errors in drawing the clock face as well as the placement of numbers and hands.[9]

ROCF copying

This test was originally developed in 1942 and it has proven to be an important neuropsychological tool to assess the visual-constructional ability. The participants were accordingly asked to copy a complex figure. In this study, the "recall" part of the test in which the figure was reproduced by memory was not assessed. According to the Taylor-Osterrieth scoring system, the figure is broken into 18 elements each one given two points if accurately drawn and properly placed. One point is further assigned to distorted or misplaced elements and half point is given if an element is both distorted and misplaced. The

missing or unrecognizable elements receive zero points. Therefore, the test is scored on a scale of 0-36.[10]

Interlocking finger test

This test was first introduced in 2003 to assess the visuospatial skills through the imitation of a series of four finger gestures without any symbolic meaning. In this respect, Moo et al found that the given test was highly associated with other tests of the parietal lobe function, particularly with the visual-constructional tests such as CDT and ROCF. For this purpose, the examiner directly faced the participants and continued to display each finger figure until the participants felt they had identically imitated it. The ability to reproduce each finger figure is scored with one point if the interlocking finger component is accurate, regardless of the position of the non-interlocking fingers or the posture of the arms. The total score ranges from zero to four.[7]

Statistical analysis

Descriptive statistics were used to examine the characteristics of the study participants. The one-way analysis of variance (ANOVA) was used to examine the differences between the groups on cognitive performance. Multivariate analysis of covariance was used to examine the effects of confounding factors. Follow-up pairwise comparisons were performed after adjustment for multiple testing (Bonferroni). The alpha level was set at 0.05 for all the statistical tests. All analyses were conducted using SPSS 14.0.

Results

A total of 92 participants including 30 patients with schizophrenia, 30 individuals suffering from MIP, and 32 normal controls participated in this study. Their demographic and clinical characteristics were further compared (Table 1), and no significant difference was found in terms of age, gender, and level of education. The group with schizophrenia showed higher severity of symptoms than the one affected with MIP according to the results of the PANSS and its subscales. Comorbid opioid use disorder was also found to be more prevalent in the group with MIP than the one suffering from schizophrenia; however, there was no significant difference between these groups of patients with regard to cannabis use disorder. In terms of medication, the patients with schizophrenia were prescribed with more anticholinergic and benzodiazepine drugs than the group with MIP (Table 1).

The results showed a significant main effect of IFT ($P<000.1$). Post hoc analysis revealed schizophrenia patients had significantly lower scores than both MIP and control groups, while the difference between controls and MIP was not significant

Regarding CDT, there was a significant main effect of group. Follow-up analysis showed there was a significant

Table 1. Demographic and clinical characteristics

	Schizophrenia (n=30)	MIP (n=30)	Control (n=32)	*P* value
Age (year), Mean±SD	36±7.6	34±7.2	33±8.7	0.41
gender male (%)	25 (83%)	26 (86%)	25 (81%)	0.84
Education, n (%)				
Elementary school	4 (13.3%)	5 (16.7%)	2 (6.3%)	
Middle school	7 (23%)	9 (30%)	10 (31%)	
High school	8 (26%)	7 (23%)	12 (37%)	0.5
Diploma	11 (36%)	7 (23%)	7 (21%)	
Bachelor or higher	0	2 (6%)	1 (3%)	
Severity of symptoms, Mean±SD				
PANSS-positive scale	13.8±4.9	11.0±4.3		0.02
PANSS-negative scale	14.1±6.3	8.0±1.5		<0.001
PANSS-general scale	27.8±5.3	25.3±5.2		0.06
PANSS-total score	55.7±10.6	44.6±7.9		<0.001
Substance, n (%)				
Cannabis	9 (30%)	27 (90%)		<0.001
Opioid	6 (20%)	9 (30%)		0.55
Medicine, n (%)				
Anticholinergic	24 (80%)	9 (30%)		<0.001
Benzodiazepine	13 (43%)	1 (3.3%)		<0.001
Sodium valproate	13 (43%)	13 (43%)		0.1
Carbamazepine	3 (10%)	0		0.2

difference only between schizophrenia and control groups, indicating schizophrenic patients had less accurate performance than controls on CDT; although, the performance of MIP group was comparable to both controls and schizophrenic patients. Similar to the IFT test, on the ROCF, there was a significant main effect of group, with schizophrenic patients exhibiting significantly lower scores than both MIP and controls. In contrast, controls and MIP group performed similarly on ROCF test (Table 2).

Given that the PANSS scores, cannabis use disorder, as well as benzodiazepine and anticholinergic drug use were different in both groups of patients, the analysis was repeated between them, considering these variables as cofounders. The effect of anticholinergics on the ROCF results and the impact of benzodiazepines on the IFT scores were further shown to be significant, with significance levels of 0.01 and 0.02, respectively. Controlling these variables, the patients with schizophrenia had more impairments once again compared with the group with MIP in the IFT and ROCF tests, and there was no significant difference between these two groups in terms of the CDT outcomes.

The scores of the neurocognitive tests were correspondingly compared across different durations and patterns of methamphetamine use and no association was observed between these scores and duration or pattern of methamphetamine use (Table 3). The data of two participants in MIP group were missing and the results of 28 patients were analyzed in the case of this association.

Discussion

The study results revealed that the group with schizophrenia had significantly greater neurocognitive deficits in two out of the three tests related to the parietal lobe, namely IFT and ROCF. However, the group with MIP showed no difference in these two tests as compared with the normal control group. In terms of the CDT test outcomes, the group with schizophrenia, unlike the patients hospitalized with MIP, suffered from significantly more impairments than the normal controls but the two groups of patients were not significantly different themselves. Despite more benzodiazepine and anticholinergic drugs prescribed for the group with schizophrenia and more common comorbid opioid dependency in the patients with MIP, controlling these variables did not change the results. Besides, there was no association between either duration or pattern of methamphetamine use and the scores of these neurocognitive tests. In terms of the severity of the symptoms, the group with schizophrenia obtained significantly higher PANSS scores despite the inclusion criteria of the total PANSS score of less than 70 for all patients. The group hospitalized with schizophrenia once again had a significantly lower performance in the IFT and the ROCF tests upon controlling PANSS score as a confounding variable. This was consistent with the findings reported in a previous study by Salo et al., in which the severity of the psychotic symptoms in patients with schizophrenia and MUD had not affected their cognitive functions.[11]

ROCF copying

Based on the ROCF results, it can be concluded that patients with schizophrenia show more impairments in visuospatial abilities than patients with MIP and control group. The results of this study are in contrast with the results of the study by Khalkhali et al showing similar scores of ROCF in schizophrenia and MIP.[6] In this regard, some differences might justify the contradiction. First, Khalkhali et al included patients with MUD and MIP

Table 2. The results of neurocognitive tests in three study groups

	Schizophrenia (S)	MIP (M)	Control (C)	Sig. (between S and M)	
IFT (Mean ± SD)	2.4 ± 0.2	3.4 ± 0.7	3.5 ± 0.5	< 0.001	(C = M) > S
CDT (Mean ± SD)	7.9 ± 2.0	8.5 ± 2.2	9.3 ± 1.6	0.02	C = M, M = S, C > S
ROCF (Mean ± SD)	27.3 ± 6.4	31.2 ± 3.7	30.6 ± 4.3	0.2	(C = M) > S

Abbreviations: IFT, Interlocking finger test; CDT, clock-drawing test; ROCF, Rey-Osterrieth complex figure.

Table 3. Duration and patterns of methamphetamine abuse and their association with neurocognitive test results

		N	IFT		CDT		ROCF	
			Mean ± SD	*P* value	Mean ± SD	*P* value	Mean ± SD	*P* value
DMA	< 6 months	6	3.1 ± 0.7	0.289	8.1 ± 2.4	0.752	31.7 ± 3.4	0.874
	6 months – 1 year	7	3.1 ± 0.8		9.0 ± 1.8		31.5 ± 4.5	
	> 1 year	15	3.6 ± 0.6		8.2 ± 2.4		30.8 ± 3.9	
PMA	Daily	20	3.6 ± 0.6	0.055	8.6 ± 2.1	0.645	31.5 ± 4.1	0.678
	Once a week or more	2	3.0 ± 0.1		7.0 ± 2.8		29.0 ± 4.2	
	Less than once a week	6	2.8 ± 0.7		8.3 ± 2.5		30.9 ± 3.1	

Abbreviations: IFT, Interlocking finger test; CDT, clock-drawing test; ROCF, Rey-Osterrieth complex figure; DMA, duration of methamphetamine abuse; PMA, pattern of methamphetamine abuse.

with at least 6-month duration of methamphetamine use and at least one-weak duration of psychosis,[6] while just MIP patients were included in the present study, even if they had been using methamphetamine for less than 6 months. Some studies have suggested that short-term acute methamphetamine use might improve visuospatial perception.[12,13] Second, Khalkhali et al assessed ROCF recall in addition to copy. ROCF recall is related to visual memory and shows moderate deficits in MUD, while ROCF copy implies visuospatial abilities and shows small to moderate deficits in MUD.[14] As MUD was not an inclusion criterion in the present study and ROCF recall was not used, there were certain differences between the results of the present study and those of the study by Khalkhali et al[6].

Interlocking finger test

Like the results of the current study on ROCF, IFT showed significantly more impairments in patients with schizophrenia than MIP group and no significant difference was found between MIP and control groups. This is a newly developed test to assess visuospatial skills which was proved in the study by Moo et al to have correlation with CDT and ROCF copy.[7] There is a lack of data on this test in both schizophrenia and MIP patients and the present study was the first to use this test for assessment of visuospatial abilities in these two groups of patients.

Clock-drawing test

In contrast with the results of the present study on ROCF and IFT that showed significantly more impairments in patients with schizophrenia than MIP group, in case of CDT, the only significant difference was between schizophrenia group and normal controls, and MIP group did not show any significant difference with other two groups. This is the first study on the use of CDT for the evaluation of neurocognitive functions in patients with MIP. One study by Zhang et al suggested lower scores on CDT in patients with schizophrenia than control group.[15] While the role of visuospatial skills in CDT seems to be more crucial and drawing the clock is used as an indicator of visuospatial skills, clock drawing involves verbally mediated cognitive processes,[9] executive functioning, and verbal working memory related to prefrontal cortex.[16] Previous studies have not shown differences between patients with schizophrenia and MIP in executive functioning and working memory.[4,5] Thus, the lack of significant difference between these two groups of patients on CDT might stem from the point that it does not purely assess the visuospatial abilities related to the parietal lobe.

In contrast with the results of the study by Jacobs et al suggesting the similarity between schizophrenia and MIP as well as possible shared neurobiology,[4] the results of the present study were in line with those of the studies advocating some differences between both disorders in spite of some similarities.[3] The findings of the present study were also compatible with the results reported by Ezzatpanah et al, suggesting the difference between schizophrenia and MIP in terms of the parietal lobe neurocognitive functions.[5] In a review study, Wearne and Cornish found more parietal lobe deficits, thought disorders, and negative symptoms in patients with schizophrenia than those with MUD.[3]

There were some limitations in this study that should be noticed. As a cross-sectional study, it suffered from its own inherent limitations. With a longitudinal design, it would be thus possible to investigate the effect of methamphetamine abstinence duration on the cognitive scores. However, in the meta-analysis by Potvin et al, the association between cognitive deficits and abstinence duration was not found significant.[14] The relatively small sample size in this study might also have not provided sufficient power to detect significant differences in terms of CDT. The patients in this study were included from one inpatient center, hence it could reduce the generalizability of the results. Among a variety of formal cognitive tests related to parietal lobe function including visual-constructional tasks (i.e. ROCF, drawing interlocking polygons -- as on the MMSE, clock drawing/setting, and IFT), visual perceptual tasks (i.e., time perception, Benton's judgement of line orientation, Raven's progressive matrices, Hooper visual organization test), right-left orientation, and arithmetic/calculations (WAIS-R performance subtest), this study focused on visual constructional tasks, so replication is essential to increase the confidence that a broad set of parietal lobe-related cognitive tests can be significantly different in schizophrenic and MIP patients.

Conclusion

Despite its limitations, this study attempted to specifically compare schizophrenia and MIP in terms of visual-constructional domain of cognitive functions related to parietal lobe. To sum up, in two out of three tests associated with this cognitive domain, namely IFT and ROCF, the patients with MIP showed significantly higher performance than the individuals affected with schizophrenia but had similar performance with the normal controls. These results might be in accordance with the neurobiology of both disorders. On the condition that the results are replicated in other studies, some parietal lobe neurocognitive tests might be considered once it is difficult to differentially diagnose schizophrenia and MIP.

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Author Contributions

Conceptualization: Navid Khalili.

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Writing – review & editing: Navid Khalili.

Conflict of Interests
The authors declare no conflict of interest in this study.

Ethics Approval
The research was conducted in accordance with the Helsinki Declaration and approved by the Committee of Ethics in Research, Kerman University of Medical Sciences under the Ethical Code IR.KMU.REC.1399.680.

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