

Prolonged Methamphetamine-Induced Psychosis: Difference With Schizophrenia

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Abstract- The main objective of the present study was to compare the distribution of underlying factors such as neurological soft signs, obstetric complications, and family history of psychiatric disorders between two groups of schizophrenic patients and patients with prolonged methamphetamine-induced psychosis. In a case-control study, 30 patients with prolonged methamphetamine-induced psychosis and 30 patients with schizophrenia were selected. Data were collected through a demographic questionnaire, the Buchanan and Heinrichs' Neurological Evaluation Scale (NES), the Lewis-Murray's Obstetric Complications Scale (LMOCS), and the Weissman's Family History Screen (FHS). Mean scores of the neurological soft signs (\pm SD) in the two groups of schizophrenic patients and patients with prolonged methamphetamine-induced psychosis were 15.7 ± 8.7 and 11.7 ± 6.2 , respectively ($P=0.040$), and a significant difference was observed in the sensory integration between the two groups ($P=0.022$). Obstetric complications revealed similar distributions in the two groups. Patients with prolonged methamphetamine-induced psychosis reported higher prevalence of alcohol and other substances use disorders ($P=0.003$ and $P=0.001$, respectively) in their close relatives; however, the distributions of other disorders were not statistically different between the two groups' close relatives. Similarities and differences in certain aspects were observed between the two groups, suggesting susceptibility for psychosis in patients with prolonged methamphetamine-induced psychosis; yet we found diversities that distinguish the two disorders.

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Introduction

Methamphetamine is a substance derived from amphetamines with strong psychotropic components (1). According to the United Nations Office on Drugs and Crime (UNODC), the amount of amphetamine-type stimulants (ATS), and specifically methamphetamine, has increased worldwide from 2008 to 2012. The annual global incidence of ATS use in people aged 15-64 years from 2008 to 2010 was 0.3–1.2% (i.e., 14.3–52.5 million people worldwide) (2).

ATS were unavailable in Iran until 2005 (3); however, considering the incidence of ATS use, Iran was ranked fifth in 2014 (4). According to reports provided by the International Narcotics Control Board (INCB), the use of stimulants is constantly increasing in Western Asia such as the increasing rate of methamphetamine use in Iran (5).

One of the manifestations of methamphetamine use is

methamphetamine-induced psychosis with similar clinical symptoms of schizophrenia (6). The clinical features of these two disorders are quite similar and differentiating them based on their clinical symptoms is a difficult process that needs to consider the history of substance use and clinical judgment (7). Unlike schizophrenia, methamphetamine-induced psychotic disorder immediately disappears after cessation of drug use in most cases (7); however, there are people who still suffer from psychosis despite the cessation of drug use or people who experience relapses of psychotic episodes after years of methamphetamine use cessation (8,9). Presumably, patients with prolonged methamphetamine-induced psychosis have a genetic susceptibility to primary psychotic disorders, such as schizophrenia (7,10). Several shared gene variants were found between patients with schizophrenia and those with methamphetamine-induced psychosis (11). Any patients

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with a primary diagnosis of substance-induced psychosis are expected to suffer from future psychotic problems (9). Studies have indicated that the close relatives of amphetamine users who experience psychotic attacks reveal a high risk of schizophrenia (6). Notably, prolonged methamphetamine-induced psychosis is not a distinct clinical problem, but is in general, a problem caused by methamphetamine use (7). Thus, people with psychotic potentiality will suffer from this disorder after methamphetamine use and their psychosis may persist longer (6).

In a study, schizophrenia risk factors were investigated in amphetamine users and it was found that psychotic patients who used amphetamine are more likely to become schizophrenic (7).

Considering the similarities between the schizophrenic and prolonged methamphetamine-induced psychotic patients, a diagnosis question arises: *Is the prolonged methamphetamine-induced psychosis a primary psychotic disorder like schizophrenia or is it a distinct phenomenon?*

DSM-5 has not clearly mentioned the timeframe for diagnosis of psychosis, and if it lasts for more than a month, it will be considered a primary psychosis. Furthermore, the symptoms of schizophrenia and prolonged methamphetamine-induced psychosis are quite similar. Therefore, the risk factors of schizophrenia were studied in patients with prolonged methamphetamine-induced psychosis and were compared with patients with schizophrenia in the present study. Additionally, in order to study the effects of the genetic factors, the histories of psychiatric disorders were analyzed in the patients' close relatives, and to assess the environmental risk factors, the patients' obstetrics and gynecological complications were examined. Neurological soft signs are endophenotypes of schizophrenia (12). In psychopathology, an endophenotype is an internal phenotype that lies in the pathway between the symptoms and genes involved in a disease. Endophenotype is related to biochemistry, endocrine, neuropsychological, neuroanatomical, and neurophysiological parameters of disease and characterizes the genes responsible for and underlying pathogenesis of disease (12-14). Therefore, the neurological soft signs were examined as endophenotypes in the present study. The core objective of the present study was to compare the distribution of the underlying factors such as neurological soft signs, obstetric labor complications, and family history of psychiatric disorders between two groups of patients with schizophrenia and patients with prolonged methamphetamine-induced psychosis.

Materials and Methods

The present study was designed as a case-control study to compare the neurological soft signs, family history of psychiatric disorders, and the obstetric complications of patients' birth. Collection of patients was from June to December 2015. Among all the patients who were referred to the Iran Psychiatric Center, Tehran, for their psychotic symptoms, including hallucinations, delusions, and disorganization in either speech or behavior, 60 patients were finally selected for this study. We used the diagnostic criteria for schizophrenia and substance-induced psychotic disorder of the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) and diagnoses were established according to the semi structured clinical interview based on DSM-IV (SCID) (15). All interviews were conducted by a well-trained senior psychiatric resident. Among the patients whose psychotic symptoms were attributed to methamphetamine usage (methamphetamine-induced psychotic disorder), the patients with psychotic symptoms lasting for more than 30 days after discontinuing methamphetamine use, were selected, based on the patients' utterance and/or urine toxicological test for amphetamine or methamphetamine. Based on the available and consecutive sampling, 30 patients with prolonged methamphetamine-induced psychotic disorder and 30 patients with schizophrenia were selected. The selected patients were aged 18-60 years. Mean age (\pm SD) was 37.6 ± 9.6 years in the methamphetamine group and 36.9 ± 10.2 years in the schizophrenia group. Sex ratio in the schizophrenia group was determined equal to methamphetamine group; hence both groups comprised 28 males and 2 females, each. In both groups, patients with suspected or well-diagnosed mental retardation or known neurological disorders and history of present or previous cannabis use were excluded. Patients with methamphetamine-induced psychotic disorder who had a previous history of any major psychiatric disorders, including psychotic or mood disorders, were also excluded. Exclusion criteria for the schizophrenia group included a history of any stimulant substance use and positive urine toxicology for amphetamine or methamphetamine. All patients and their legal guardians signed an informed consent. The protocol of the study was confirmed by the ethical board of Iran University of Medical Sciences (project no. 24153).

In data collection process, demographic information, including age and sex of patients, season of birth, maternal and paternal ages at birth, birth order, number of siblings, patient education and marital status, and

information about substance use were collected.

Neurological evaluation was performed using the Neurological Evaluation Scale (NES) presented by Buchanan and Heinrichs in 1989 for the standard assessment of neurological impairments in schizophrenia patients and discriminated them from the nonpsychiatric controls (16). This scale is composed of 26 items; most of these scored on the three-point scale: 0 for absent impairment, 1 for mild impairment, and 2 for marked impairment. Some items scored on a two-point scale: 0 for absent and 2 for marked positive findings. Scoring was done by trained clinicians. Three subscales (sensory integration, motor coordination, and sequencing of complex motor acts) are defined and other items assess the cerebral dominance, primitive reflexes, and frontal lobe disinhibition, short-term memory, eye movements, and other aspects of cerebral functions. Items for cerebral dominance are omitted in the total scoring of NES. Validity and interrater reliability of the scale were reported. The intraclass correlation coefficient of the scale was reported as 0.95.

Obstetric complications were assessed by Lewis-Murray Obstetric Complication Scale (LMOCS). It includes 4 antenatal and 11 intranatal events based on a three-point scale: 0 for no event, 1 for equivocal event, and 2 for definite event. No total score is reported. We merged the equivocal and definite events to compare the two groups. The scale is completed by a clinician through interviewing mothers or other informants. We excluded items that the participants did not remember. This scale is widely used in different population, including patients with schizophrenia and has good reliability and validity (17).

To evaluate the family history of common and major psychiatric disorders, we used clinical interview based on the Family History Screen (FHS), prepared by Weissman (18). In this interview, we evaluated 15 classes of psychiatric disorders and suicidal behaviors. We considered the information about patients' parents, siblings, grandfathers/grandmothers, and children. Each interview lasted about 20 min. The questionnaire was translated to the Persian language by the research group, and face and content validity of the questionnaire was confirmed by five staff psychiatrists.

Statistical analysis

Data analysis was done using IBM SPSS Statistics (SPSS Inc., Chicago, Illinois). To describe the qualitative variables, frequencies were reported. For quantitative variables; mean, standard deviation, median, and range

were documented. Student's t-test was used to compare the means for age variables and the NES scores. Patients' education (ordinal variable) and number of siblings and birth order did not reveal normal distribution and the two groups were compared by Mann-Whitney U test. Chi-square test was performed to compare the data distributions for marital status and season of birth. Items of the LMOCS were compared by Fisher's exact test. Type I error (α) was set at 0.05.

Results

No statistically significant difference was observed between the two groups in case of mean ages of parents at child's birth (Table 1). The distributions of the birth season, marital status, and education level were not statistically different between the two groups (Table 2). The medians of the number of siblings in the patients with schizophrenia and in the patients with prolonged methamphetamine-induced psychosis were 4.5 (range: 0-10) and 5 (range: 2-9), respectively ($P=0.631$). The median rank of birth was 3 in patients with schizophrenia (range: 0-8) and 3 in prolonged methamphetamine-induced psychosis (range: 1-8) ($P=0.846$). The medians of the number of hospitalizations in the patients with schizophrenia and in the prolonged methamphetamine-induced psychotic patients were 2 (range: 1-10) and 5 (range: 1-5), respectively ($P=0.045$). The mean ages of the first psychotic episode (\pm SD) in the patients with schizophrenia and in the prolonged methamphetamine-induced psychosis were 24.3 ± 6.3 years (median=23, range: 17-46 years) and 33 ± 10.5 years (median=30, range: 15-57 years), which indicates a significant difference ($P<0.001$).

Neurological soft signs

The mean scores of the neurological soft signs in the two groups of patients with schizophrenia and prolonged methamphetamine-induced psychosis were 15.8 ± 8.7 (median=16, range: 4-36) and 11.7 ± 6.2 (median=12.5, range=3-25), respectively (t-test results: $t=2.104$; $P=0.040$). Subgroups of neurological soft signs were compared between the two groups (Table 3). The results indicated a significant difference between the two groups in the left-right confusion disorder ($\alpha=0.05$); however, with the increase of α level to 0.1, the differences in the extinction and gaze impersistence were statistically significant between the two groups.

Table 1. Patients' age and their parental age (years) at the time of the patients' birth in both groups

	Schizophrenia			Prolonged methamphetamine-induced psychosis			T-test	
	Mean±SD	Median	Range of variation	Mean ±SD	Median	Range of variation	t	P
Father's age	33.9±6.8	33	24-46	34.1±10.3	31	18-53	0.075	0.941
Mother's age	25.4±7.0	24	14-44	27.7±9.8	24.5	13-52	1.014	0.315

Table 2. The distributions of gender, time of birth, marital status, and education level in both groups (%)

		Schizophrenia	Prolonged methamphetamine-induced psychosis	Chi-square test	
				X ²	P
Season of birth	Spring	6 (20)	5 (17)	4.081	0.253
	Summer	7 (23)	11 (37)		
	Autumn	10 (33)	4 (13)		
	Winter	7 (23)	10 (33)		
Marital status	Married	6 (20)	12 (40)	2.875*	0.091
	Single	17 (57)	13 (43)		
	Divorced	6 (20)	4 (13)		
	Widow	1 (3)	1 (3)		
Education	Illiterate	2 (7)	0 (0)	0.583**	
	Elementary	4 (13)	3 (10)		
	High school	14 (47)	16 (53)		
	High school diploma	7 (23)	6 (20)		
	University	5 (17)	3 (10)		

*Married in comparison to the other groups

**The Mann-Whitney U test

Table 3. Patients' scores in subgroups of neurological soft signs in both groups

Neurological soft signs	Schizophrenia		Prolonged methamphetamine-induced psychosis		T-test	
	μ±SD	Median	μ±SD	Median	t	P
Sensory integration	3.7±2.9	3.5	2.2±1.8	2	2.368	0.022
Motor coordinate	1.5±1.4	2	1.6±1.4	1	0.278	0.782
Sequencing of complex motor task	4.4±2.5	4.5	3.2±2.7	3.5	1.786	0.079
Others	6.1±3.0	6	4.6±3.0	4	1.923	0.059
Total score	15.8±8.7	16	11.7±6.2	12.5	2.104	0.040

Obstetric complications

In the patients with schizophrenia, the data related to the obstetric complications were obtained either from mothers (20 cases) or from other sources (6 cases) and 4 cases were not available to provide information. Concerning the patients with prolonged methamphetamine-induced psychosis, the data were obtained either from mothers (20 cases) or from the patient's relatives (8 cases) and 2 cases were not available to provide information. No cases of infection during pregnancy (e.g., rubella, syphilis, and HIV), Rh incompatibility, cord collapse, unusual or breach presentation of the fetus, and use of incubator for more than 4 weeks, were observed in any of the groups. The

distributions of child labor accidents were not significantly different between the two groups (Table 4) and none of the mothers in both groups used any specific medication during their pregnancy.

Family history of psychiatric disorders

The two groups' family histories of psychiatric disorders were almost similar (Table 5); however, patients with persistent methamphetamine-induced psychosis reported higher prevalence of alcohol (P=0.003) and other substances (P=0.001) use disorders in their close relatives.

Table 4. The distributions of child labor accidents in both groups (%). Cases of insufficient information were eliminated from the analysis

		Schizophrenia (n = 26)	Prolonged methamphetamine- induced psychosis (n = 28)	Chi-square test	
				X ²	P
Preeclampsia		1 (4)	1 (4)	0.003	1.000
APH or threatened abortion		-	2 (7)	1.929	0.491
Premature rapture of membrane		1 (4)	-	1.097	0.481
Labour >36 or <3		1 (4)	5 (18)	2.680	0.194
Twin birth complicated		1 (4)	-	1.097	0.481
Gestational age >42 or <37		1 (4)	1 (4)	0.003	1.000
Caesarean, complicated or emergency		1 (4)	3 (11)	0.927	0.612
High or difficult forceps		2 (8)	-	2.237	0.227
Birth weight <4.12 Pound (2000 g)	Insufficient information	1 (4) 7 (27)	1 (4) 5 (18)	0.003 -	1.000 -
Gross physical anomaly		- 7 (28)	1 (4) 5 (18)	0.946 0.776	1.000 0.514
Home birth	Insufficient information	1 (4)	-	-	-

Table 5. The distribution of family history of psychiatric disorders in both groups (%)

Family history of psychiatric disorders	Schizophrenia	Prolonged methamphetamine-induced psychosis	Chi-square test	
			X ²	P
Depressive disorder	7 (23)	11 (37)	1.270	0.260
Bipolar disorder	2 (7)	1 (3)	0.351	0.554
Panic disorder	2 (7)	4 (13)	0.741	0.389
Generalized anxiety disorder	6 (10)	4 (13)	0.480	0.488
Agoraphobia	2 (7)	2 (7)	-	-
Specific phobia	5 (17)	8 (27)	0.884	0.347
Social phobia	3 (10)	3 (10)	-	-
Obsessive-compulsive disorder	7 (23)	4 (13)	1.002	0.317
Psychotic disorder	6 (20)	8 (27)	0.373	0.542
Alcohol use disorder	1 (3)	10 (33)	9.017	0.003
Other substance use disorder	6 (20)	19 (63)	11.589	0.001
Antisocial personality disorder	-	2 (7)	2.069	0.159
Separation anxiety disorder	1 (3)	3 (10)	1.071	0.301
Conduct disorder	-	4 (13)	2.286	0.112*
Hyperactivity	3 (10)	6 (20)	1.179	0.2278
Suicide	1 (3)	3 (10)	1.071	0.301

*Fisher's exact test

Discussion

This study was one of the few studies that compared

the risk factors of prolonged methamphetamine-induced psychosis with schizophrenia. The results specified no significant difference between the two groups of patients

Prolonged methamphetamine-induced psychosis

in the birth season, marital status, and education level indicating demographic similarities between the two groups.

There is a lot of consideration for perinatal mental health and the consequence of perinatal problems on mother and child but there is so much for clarifying in this field (19). Regarding the obstetric complications, no significant difference was observed between the two groups; however, since the patients did not have obstetric certificates and the required data were collected through interviews with mothers, or other family members in case of mothers' death, data may be influenced by recall bias mentioned in another study by McIntosh (20). Cannon referred to the limitations of examining this factor as well (21). Thus, due to issues such as error of recall bias, the data may be not highly reliable. In studies by Lewis and Murray and Guerra, nerve damages in the developmental system, caused by obstetric complications, that lead to a person's potentiality for schizophrenia, were discussed (17,22). Lewis and Murray mentioned 5 obstetric complications related to schizophrenia: premature rupture of membranes (PROM), birth weight below 2500 gr, gestational age below 38 weeks, the use of forceps during delivery, and more than 4 weeks of incubation (17). Despite no significant difference observed in the obstetric complications between the two groups, notably, the frequencies of these complications were very low in the patients with schizophrenia; however, considerable frequency of either prolonged or fast delivery was observed (18%). Nonetheless, due to the lack of a healthy control group in the present study, we could not conclude the relationship between prolonged and fast delivery and the emergence of prolonged methamphetamine-induced psychosis. Noticeable frequencies of birth at home in the two groups of patients with schizophrenia (18%) and patients with persistent methamphetamine-induced psychosis (28%) were observed, which were comparatively higher than the present frequency of child birth at home in Iran (0.8% in urban areas and 5.4% in rural areas) (23). Presumably, delivery at home was much more frequent 30-40 years ago, therefore, its frequency should not be different from that of the controls with the same age. The low frequency of some of these complications can also be attributed to the small sample size and error of recall bias. Therefore, the observed similarities between the two groups of patients in obstetric complications might be due to the primary damages to the development of the nervous system in patients with prolonged methamphetamine-induced psychosis; however, more studies and evidences are warranted.

The results regarding the family history of psychiatric disorders indicated that other than alcohol and other substances use disorders, no other significant difference was observed between the two groups. The data of close relatives' history of psychiatric disorders were mostly collected through interviews, specifically with mothers; therefore, they cannot be considered as highly reliable data. In a study, Chen *et al.*, concluded that the morbidity rate of schizophrenia is significantly higher in the close relatives of patients with prolonged methamphetamine-induced psychosis compared to the close relatives of patients without or with short-term psychotic symptoms (6). They also stated that when the incidence of schizophrenia is higher in a patient's close relatives, he or she will be more likely to experience severe psychotic relapses with longer duration (6). Tsuang, in his study, found that the drug users with persistent psychosis had family histories of psychiatric disorders similar to that of the patients with schizophrenia (24). Chen *et al.*, proposed that the drug users with higher potentiality of psychosis, probably experience more psychotic relapses for a longer time (6).

Consistent with the results, Pickens and Milne stated that substance use disorders are more common among the close relatives of substance users and this family transmission of drug abuse is due to both genetic and environmental factors (25,26). Thus, it can be concluded that despite the fact that the family histories of psychiatric disorders were similar between the two groups, the potentiality of alcohol and substance use disorders was distinct from the potentiality of psychosis.

A significant difference was observed in the neurological soft signs scores between the two groups. The mean score of NES was higher in patients with schizophrenia compared to patients with prolonged methamphetamine-induced psychotic disorder. Nevertheless, the NES scores obtained by patients with prolonged methamphetamine-induced psychosis were also high. Notably, lack of a control group in the present experiment limited an appropriate interpretation of the results. In a study conducted in Iran on patients with schizophrenia, the mean NES scores of patients and control group were 17.6 ± 8.4 and 4.8 ± 3.55 , respectively (27). Similarly, in another study, Buchanan and Heinrichs reported the mean NES scores of patients with schizophrenia (17.42 ± 7.52) and their control group (9.6 ± 4.38) (16). As noted by Bombin, neurological soft signs may be influenced by race and ethnicity (28); therefore, results of the present study cannot be compared to the results obtained by Buchanan and Heinrichs. Therefore, the data interpretation is somehow restricted;

however, it seems that the mean NES score obtained by the patients with prolonged methamphetamine-induced psychosis lies between the NES mean scores observed in patients with schizophrenia and healthy people, including the Iranian population.

Considering the analysis of subgroups of neurological soft signs, a significant difference was observed between the two groups in sensory integration and it was more defective in the patients with schizophrenia. According to previous studies, sensory integration represents parietal lobe functions (29) and defects in heteromodal cortex (30) and is related to cognitive deficits, executive functions (13), and negative symptoms of a disease (29). As it was indicated by Tomiyama, patients with prolonged methamphetamine-induced psychosis reveal less negative symptoms than patients with schizophrenia (31). Smith reported a positive relationship between the neurological soft signs and negative symptoms (30). Regarding negative symptoms, it seems that the neurological bases of the two disorders differ. Chan found a relationship between sensory integration and cognitive disorders in the patients with schizophrenia (13). Jacobs compared cognitive neurological function between patients with paranoid schizophrenia and patients with methamphetamine-induced psychosis and found no significant difference (32); however, notably in the aforementioned study, the sample size was small and patients with methamphetamine-induced psychosis did not experience prolonged psychosis. Methamphetamine use can cause cell apoptosis, activation of multiple death pathways (33), and parietal lobe damages (34,35); nonetheless, these damages are not similar to the damages caused by schizophrenia.

Despite the studies mentioned here, it is not still clear if the neurological soft signs observed in patients with prolonged methamphetamine-induced psychosis are due to methamphetamine use and its subsequent environmental effects on the brain or due to a kind of genetic-based susceptibility for psychosis or both. And there is unclear that the chronicity of the illness in patients with schizophrenia can interfere with the result as Basseda *et al.*, found the cognitive differences between first episode schizophrenia and chronic schizophrenia (36).

In patients with persistent methamphetamine-induced psychosis, the VNTR (variable number tandem repeat) polymorphism in the dopamine transporter gene (DAT) is related to prolonged methamphetamine-induced psychosis (37) and is also influential in the emergence of schizophrenia (38). Many shared genes between the prolonged methamphetamine-induced psychosis and

schizophrenia have been proposed including the *DTNBP1* (39,40) and the *G72* that are involved in both schizophrenia (41) and methamphetamine-induced psychosis (42); however, genes exist that are not shared between the two disorders; for example, the roles of *NRG* and *DRP* (two of the important genes in schizophrenia) are not identified yet in methamphetamine-induced psychosis (43,44). Two genes, *FZD3* and *ProKR2*, involved in developmental processes are related to methamphetamine-induced psychosis; thus, it can be proposed that the existence of specific variants in such genes evolutionarily may predispose a person to methamphetamine-induced psychosis (11).

To conclude, it seems that there exist differences between the two disorders regarding neurological deficits, neurocognitive deficits, genetics, and disease symptoms indicating a need for more studies.

A point that was significantly different between the two groups was the age of psychosis onset that was considerably higher in patients with prolonged methamphetamine-induced psychosis. The beginning of substance use is probably the most influential factor in the onset of the prolonged methamphetamine-induced psychosis while in schizophrenia, inherent and neuropathologic features determine the onset of the disease. Notably, patients with prolonged methamphetamine-induced psychosis have a predisposition to psychosis, and methamphetamine use at any time of life will activate that predisposition and lead to the emergence of psychosis.

There were limitations in collecting information because of limited sample size. Lack of healthy control group and recall bias in assessing birth complications and family history of psychiatric disorders are another limitations of the study. Neuroleptics impact the prevalence of neurological soft signs (45); however, the effects of drugs were not measured and controlled in this study. Moreover, the subjects were patients with severe or chronic psychiatric diseases selected from a single referral center; thus, they could not be considered as a sample of the whole Iranian population.

The two examined groups were similar in most of the risk factors (genetic-based, family-based, and environmental factors). Significant differences were observed between the two groups regarding neurological soft signs. Notably, the overall score of patients in the neurological soft signs is generally higher than the overall score of healthy individuals; thus, it can be concluded that patients with prolonged methamphetamine-induced psychosis have a susceptibility for psychosis activated by the use of methamphetamine.

Prolonged methamphetamine-induced psychosis

It is recommended to conduct studies with larger sample sizes and patients experiencing the first episode of methamphetamine-induced psychosis, a control group consisting of healthy people, and patients with temporary methamphetamine-induced psychosis to compare and analyze their diseases' histories and risk factors in the three groups.

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