RESEARCH ARTICLE

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The Theory of Mind and Psychotic Symptoms Phenomenology in Substance-Induced Psychotic Disorder and Schizophrenia

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ABSTRACT

Objective: The study aimed to determine clinical indicators that could be used to differentiate between patients diagnosed with substance-induced psychotic disorder (SIPD) and patients diagnosed with schizophrenia by comparing their psychotic symptoms and theory of mind (ToM).

Methods: The study included 43 male patients diagnosed with schizophrenia according to DSM-5 criteria and 43 male patients diagnosed with SIPD. The patients were administered the Sociodemographic and Clinical Data Form, Scale for the Assessment of Positive Symptoms (SAPS), Scale for the Assessment of Negative Symptoms (SANS), Psychotic Symptom Evaluation Scale (PSYRATS), and Reading the Mind in the Eyes Test (RMET).

Results: In patients diagnosed with schizophrenia, the scores on SAPS subscales for structural thought disorder and bizarre behavior, as well as SANS total scores, were significantly higher compared to patients diagnosed with SIPD ($z=2.679$, $p=0.007$; $z=2.984$, $p=0.003$; $z=6.916$, $p<0.001$). The scores for recognizing negative and neutral expressions on the RMET were significantly higher in patients with SIPD than in patients with schizophrenia ($z=3.540$; $p<0.001$; $z=4.404$, $p<0.001$). It was found that as the scores on the SANS total and Affect Blunting or Flattening subscale, as well as the scores on the SAPS Bizarre Behavior subscale decrease, the probability of having SIPD increases.

Conclusion: In patients diagnosed with SIPD, there are fewer disorganized and negative symptoms compared to patients diagnosed with schizophrenia. Patients with SIPD can recognize negative and neutral expressions better than patients with schizophrenia. When making a differential diagnosis between SIPD and schizophrenia, as blunting in affect, total negative symptoms, and severity of bizarre behavior decrease, the probability of being diagnosed with SIPD increases relative to the probability of being diagnosed with schizophrenia.

Keywords: Schizophrenia, Substance-Induced Psychosis, Theory Of Mind, Psychotic Symptoms

INTRODUCTION

Psychotropic substance use can lead to various mental disorders, including substance-induced psychotic disorder (SIPD), in individuals (Keshavan & Kaneko, 2013). According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), this diagnosis is characterized by the presence of hallucinations and/or delusions that are thought to be caused by the physiological effects of the substance and cannot be better explained by another psychotic disorder, occurring during or immediately after substance intoxication or withdrawal (American Psychiatric Association, 2013). In the DSM-5 classification, psychotic symptoms in SIPD should not persist for more than 4 weeks. The time criterion for SIPD differs between the ICD-10 and DSM-5 classifications. According to the ICD-10, psychotic symptoms can persist for up to 6 months after the last substance use. Initially, it is challenging to definitively diagnose SIPD based on these criteria, and longitudinal monitoring is considered necessary to clarify the diagnosis (Beckmann et al. 2019). Some studies have concluded that substance-induced psychotic disorders do not have a specific psychopathology triggered by the substance (Chaudhury et al. 2016). The similarities between SIPD and schizophrenia in terms of positive symptoms, the frequent co-occurrence of substance use with both diseases, and the bidirectional causal relationship between substance use and psychotic symptoms further complicate the diagnostic difficulty

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of SIPD (Wilson et al. 2017) (Aldemir et al. 2018). While the differential diagnosis between SIPD and schizophrenia is challenging, making a proper differential diagnosis is critical for the management and treatment of both disorders (Cambra et al. 2023) (Fiorentini et al. 2021). Many studies have reported that negative and disorganized symptoms are less frequently observed in SIPD compared to schizophrenia, whereas positive symptoms such as delusions and hallucinations are believed to be similar in both disorders (Wilson et al. 2018). Most studies examining the differences in positive symptoms between SIPD and schizophrenia have utilized the Scale for the Assessment of Positive Symptoms (SAPS) and the Positive and Negative Syndrome Scale (PANSS). Both scales evaluate psychotic symptoms in terms of frequency, severity, and impact on the individual's functioning (Erkoç et al. 1991). The Psychotic Symptom Rating Scales (PSYRATS) assess delusions and hallucinations based on various dimensions, including content, duration, and distress severity caused by these symptoms (Haddock et al. 1999).

Theory of Mind (ToM) is defined as the ability to understand the intentions behind others' behaviors, perceive their mental states, and make predictions about their observed actions (Premack & Woodruff, 1978). This ability is associated with emotion recognition (Sebastian et al. 2012). One of the most commonly used tests for assessing this function is the Reading the Mind in the Eyes Test (RMET) (Sprong et al. 2007).

It has been shown that ToM skills are impaired in schizophrenia (Weng et al. 2022), and the performance in ToM tasks is associated with positive, negative, and disorganized symptoms (Brüne, 2005) (Bliksted et al. 2019) (Bora, 2019).

It has been shown that social cognitive functions, such as ToM and emotion recognition, are impaired in individuals with Substance Use Disorder (SUD) and SIPD (Sanvicente-Vieira et al. 2017). A study comparing the social cognitive impairments in individuals with SUD and SIPD reported a higher level of impairment in those with SIPD (Anne et al. 2018). However, research examining ToM abilities in individuals with SIPD is limited.

In our study, positive symptoms in patients diagnosed with SIPD and patients diagnosed with schizophrenia without substance use were compared, including dimensional features, in an attempt to understand the differences in positive symptomatology that are often predicted but not clearly identified through clinical observations. Additionally, the ToM abilities of both groups were investigated. Based on the belief that ToM impairments are a structural characteristic of schizophrenia (Irani et al. 2006) and that there is a relationship between psychotic symptoms and ToM (Brüne, 2005), the ToM abilities and psychotic symptoms were compared in both disorders. The aim was to identify helpful clinical indicators for the differential diagnosis between patients with SIPD and patients with schizophrenia without substance use.

METHODS

Between September 2020 and January 2021, a total of 43 male patients diagnosed with schizophrenia according to DSM-5 diagnostic criteria, and 43 male patients diagnosed with SIPD who were receiving inpatient treatment at the units affiliated with Istanbul Bakırköy Prof. Dr. Mazhar Osman Mental Health and Neurological Diseases Hospital, aged 18-50 years, were included in the study. The study was approved by the Bakırköy Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee with decision number 2020-18-16 on September 7, 2020. This article is derived from the dissertation entitled "Phenomenological evaluation of the psychiatric symptoms of patients with a diagnosis of psychotic disorder due to pam use and patients with a diagnosis of schizophrenia without pam use and their relationship with theory of mind". The patients were informed about the study and written consent was obtained for their participation. Exclusion criteria were illiteracy, intellectual disability, dementia, and other organic mental disorders that could hinder the effective completion of the research battery. Based on examinations conducted by at least 2 psychiatric specialists, along with old medical records and information obtained from the patients and their relatives, a total of 58 patients admitted with a diagnosis of schizophrenia and 57 patients admitted with a diagnosis of SIPD were evaluated. Patients diagnosed with schizophrenia, whose known duration of illness was less than 10 years and who had not used a psychotropic substance in the last 5 years were included in the sample by verifying their medical records and information obtained from the patients and their relatives.

The patients included in the study were evaluated at an average of 72 hours after admission to avoid potential confusion caused by substance intoxication symptoms. Based on this evaluation, 8 patients diagnosed with SIPD were not included in the study because they continued to experience psychotic symptoms during the 4-week period without psychotropic substance use. Patients diagnosed with psychotic disorders related to cannabinoid, synthetic cannabinoid (SC), methamphetamine (MA), ecstasy, and cocaine use were included in the study. However, 4 patients diagnosed with psychotic disorders related to opioid, inhalant, and alcohol use were not included in the study due to the potential confusion caused by withdrawal and intoxication symptoms in evaluating psychotic symptoms. Among the patients diagnosed with schizophrenia, 4 patients, and among those diagnosed with SIPD, 2 patients were not included in the study as their clinical presentation was characterized by significant mood disturbances rather than psychotic symptoms, suggesting a closer diagnosis to bipolar and related disorders. Patients diagnosed with comorbid psychotic disorders and SUD were excluded based

on their medical records and information obtained from the patients and their relatives. In selecting these patients, it was taken into account that psychotic symptoms persist for a significant period during substance use and after the cessation of withdrawal, and that there are recurrent periods in the course of the illness that are not attributed to substance use. As a result of this evaluation, 7 patients diagnosed with schizophrenia were not included in the study as their medical records, previous test results, and family history indicated that they had used a psychotropic substance at least once in the last 5 years, which could potentially lead to confusion. Four patients diagnosed with schizophrenia were also not included in the study due to their known illness duration being over 10 years.

The hypotheses of the study are as follows;

1. There are differences in the dimensional features of delusions and hallucinations between patients diagnosed with SIPD and patients diagnosed with schizophrenia without psychotropic substance use.
2. Negative and disorganized symptoms are less common in patients diagnosed with SIPD than in patients diagnosed with schizophrenia without psychotropic substance use.
3. The ToM abilities of patients diagnosed with SIPD are better than those of patients diagnosed with schizophrenia without psychotropic substance use.

Instruments

Sociodemographic and Clinical Data Form: Prepared by the authors in line with the objectives of the study and evaluated based on the information obtained from the participants.

Scale for the Assessment of Positive Symptoms (SAPS): SAPS, developed by Andreasen, is a scale designed to measure the level, distribution, and severity of positive symptoms in schizophrenia. It includes four subscales: hallucinations, delusions, bizarre behavior, and positive formal thought disorder, with a total of 34 items (Andreasen 1984a). The Turkish validity and reliability study of the scale was conducted by Erkoç and colleagues (Erkoç 1991a).

Scale for the Assessment of Negative Symptoms (SANS): The SANS, developed by Andreasen, aims to assess the level, distribution, and severity of negative symptoms in schizophrenia. It consists of five subscales: affective flattening, alogia, apathy, anhedonia, and attentive impairment, with a total of 25 items (Andreasen 1984b). The Turkish validity and reliability study of the scale was conducted by Erkoç and colleagues (Erkoç 1991b).

Psychotic Symptom Rating Scale (PSYRATS): It is composed of a semi-structured interview form and a scoring chart developed by Haddock et al. to assess auditory hallucinations and delusions. It is treated as two separate scales. The Auditory Hallucinations Scale consists of 11 items, while the Delusions Scale consists of 6 items (Haddock et al. 1999). This scale has been adapted to the Turkish sample by O.M. Sevi et al. (Sevi, 2016).

Reading the Mind in the Eyes Test (RMET): The RMET, developed by Baron-Cohen et al. consists of 36 photographs that include only the eye region of actors or actresses (Baron-Cohen et al. 2001). The Turkish validation and reliability study of the test was conducted by Yıldırım et al. After removing 4 items with low internal consistency in the Turkish version, it consists of 32 items (Yıldırım et al. 2011).

In this test, individuals make inferences about the mental state of the person in the picture by looking at images with eyes displaying various expressions. Participants are asked to choose the option that best describes the mental state of the person in the picture from the provided 4 choices. The options do not only include the five basic emotions of fear, sadness, anger, happiness, and disgust, but also encompass complex emotions and intentions. Therefore, the test is considered as an indicator of ToM ability rather than emotion recognition (Bedi et al. 2010).

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA) statistical software package. Descriptive statistics were reported as the number of units (n), percentage (%), mean ± standard deviation (mean ± sd), median (M), minimum (min), maximum (max), and interquartile range (IQR) values. The normal distribution of data for numerical variables was assessed using the Shapiro-Wilk normality test. The homogeneity of variances was evaluated using the Levene test. Group comparisons for numerical variables were performed using independent samples t-test when the data followed a normal distribution, and Mann-Whitney U test when the data did not follow a normal distribution. Pearson chi-square test was used for comparing groups on categorical variables. Variables with $p<0.25$ in univariate analyses were considered as confounding factors. The interrelationships between scales were examined using Spearman's correlation analysis. The effect of scale scores on schizophrenia was assessed using both univariate and multivariate binary logistic regression, and the final model was determined using the backward Wald elimination method. The predictive performance of scale scores for schizophrenia was evaluated using Receiver Operator Characteristic (ROC) curve analysis. Prior to ROC curve analysis, propensity score matching was conducted to account for confounding factors present in the study. A p-value <0.05 was considered statistically significant.

RESULTS

Sociodemographic Characteristics of Participants

Our study included 43 male patients diagnosed with schizophrenia and 43 male patients diagnosed with SIPD. The mean age of the SIPD-diagnosed patients was 31.23±4.9, while the mean age of the schizophrenia-diagnosed patients was 33.5±7.9. There was no statistically significant difference found in terms of mean age (t=-1.615, p=0.111), marital status (χ^2=4.643, p=0.125), and education level (χ^2=5.125, p=0.173) between the two groups (Table-1).

Assessment of Substance Use Characteristics in Patients Diagnosed with SIPD

The average age of the SIPD patients evaluated in the study was found to be 16.67±28.00, and the age of substance use initiation among the participants ranged from 6.00 to 28.00. Among the SIPD patients, 26 (60.5%) had a history of MA use, 42 (97.7%) had used cannabinoids, 32 (74.4%) had used SC, 24 (55.8%) had used ecstasy, 39 (93%) had a history of multiple psychotropic substance use, and 14 (32.6%) had used cocaine (Table-2).

Comparison of Scale Scores Between Groups

In the SIPD group, scores for bizarre behavior and positive formal thought disorder were found to be significantly lower than those in the schizophrenia group (p=0.003, p=0.007). Additionally, in the SIPD group, scores for blunted or flattened affect, alogia, diminished energy and interest, anhedonia, and social withdrawal in the SANS scale were statistically lower compared to the schizophrenia group (p<0.001), while scores for negative affect, neutral affect, and total scores in the RMET scale were statistically higher than those in the schizophrenia group (p<0.001) (Table-3).

Logistic Regression Results for Factors Influencing the Probability of SIPD

Variables with p<0.25 among sociodemographic factors (age, education level, marital status) were considered confounding

Table 1. Comparison of Descriptive Characteristics of the Groups

	Groups		Test Statistics		
	SIPD n=43	**Schizophrenia n=43**	**Test Value**	**p**	**Effect Size**
Age, (years)					
mean±sd	31.2±4.9	33.5±7.9	t=1.615	0.111	0.35
min-max	20-45	18-47			
Marital Status, n (%)					
Single	26 (60.5)	35 (81.4)	χ^2=4.643	0.125	0.42
Married	12 (27.9)	5 (11.6)			
Divorced/widowed	5 (11.6)	3 (7.0)			
Education Level,n (%)					
Primary school	16 (37.2)	15 (34.9)	χ^2=5.125	0.173	0.44
Middle school	23 (53.5)	16 (37.2)			
High school	3 (7.0)	8 (18.6)			
University and above	1 (2.3)	4 (9.3)			

t: Independent sample t-test, χ^2: Chi-square test
SIPD:Substance-induced psychotic disorder

Table 2. Substance Use Characteristics of Patients Diagnosed with SIPD

	SIPD n=43	**Mean±Sd.**	**Min.-Max.**
Age of Onset of Substance Use		16.67±28.00	6.00-28.00
Substance Use Status		**n**	**%**
Cannabinoid		42	97.7
Synthetic Cannabinoid (SC)		32	74.4
Ecstasy		24	55.8
Methamphetamine (MA)		26	60.5
Cocaine		14	32.6
Multiple Substance Use		39	93

SD: Standard Deviation, SIPD:Substance-induced psychotic disorder

Table 3. Comparison of Scale Scores by Groups

	Groups				Test Statistics	
	SIPD		Schizophrenia		z value	p value
	M	IQR	M	IQR		
SAPS						
Hallucinations	16.0	12.0	14.0	10.0	1.012	0.312
Delusions	23.0	13.0	24.0	17.0	0.899	0.368
Bizarre Behaviour	5.0	4.0	7.0	6.0	2.984	**0.003**
Positive Formal Thought Disorder	7.0	6.0	13.0	8.0	2.679	**0.007**
SAPS, Total	53.0	26.0	58.0	27.0	1.248	0.212
SANS						
Affective Flattening or Blunting	4.0	7.0	18.0	9.0	7.016	**<0.001**
Alogia	3.0	5.0	12.0	6.0	7.133	**<0.001**
Unwillingness-Apathy	5.0	3.0	13.0	6.0	7.250	**<0.001**
Anhedonia-Asociality	8.0	3.0	16.0	6.0	6.679	**<0.001**
Attention	2.0	3.0	3.0	2.0	2.223	**0.026**
SANS, Total	23.0	16.0	63.0	23.0	6.916	**<0.001**
PSYRATS						
Auditory hallucinations	20.0	18.0	21.0	23.0	0.347	0.729
Delusions	17.0	5.0	18.0	6.0	1.648	0.099
PSYRATS, Total	37.0	21.0	42.0	28.0	0.445	0.656
RMET						
Positive Affect	3.0	2.0	3.0	2.0	0.489	0.625
Negative Affect	6.0	2.0	4.0	3.0	3.540	**<0.001**
Neutral Affect	10.0	5.0	7.0	3.0	4.404	**<0.001**
RMET,Total	18.0	7.0	14.0	6.0	4.095	**<0.001**

z: Mann-Whitney U test, p<0.05 value was considered statistically significant., SAPS: Positive Symptoms Evaluation Scale, SANS: Negative Symptoms Evaluation Scale, PSYRATS: Psychotic Symptom Evaluation Scale, RMET: Mind Reading Test from the Eyes, SIPD:Substance-induced psychotic disorder

factors and included in the model as correction factors. Table 4 presents the results of binary univariate logistic regression analysis regarding the factors influencing the risk of SIPD. To determine the final factors affecting the disease condition, two different multivariate binary logistic regression models were constructed, taking into account highly correlated variables (Table-5).

The first model included SAPS; Hallucinations, Bizarre Behavior, Positive Formal Thought Disorder, SANS; Blunted or Flattened Affect, Attention, RMET; Negative Affect, Neutral Affect variables. The Backward Wald method was used to determine the final variables. As a result of Model-1, SAPS Bizarre Behavior and SANS Blunted or Flattened Affect dimensions were found to have an effect on the disease groups. The risk of substance psychosis increases by 1.421 times as the SAPS Bizarre Behavior score decreases by one unit, and by 1.452 times as the SANS Blunted or Flattened Affect score decreases by one unit (Table-5).

In Model-2, SAPS; Hallucinations, Bizarre Behavior, Positive Formal Thought Disorder, SANS Total, RMET Total scores were included in the analysis. The analysis results showed that SAPS Bizarre Behavior and SANS Total scores had an effect on the disease groups. As the SAPS Bizarre Behavior score decreases by one unit, the risk of substance psychosis increases by 1.594 times, and as the SANS Total score decreases by one unit, the risk of substance psychosis increases by 1.146 times (Table-5).

Evaluation of the Performance of Scale Scores in Predicting SIPD Diagnosis through ROC Curve Analysis

Propensity score matching was conducted before performing ROC curve analysis due to the presence of confounding factors in the study. For SAPS Bizarre Behavior, the area under the curve (AUC) value was 0.813, the optimum cut-off point was <7.0, sensitivity was 78.1%, and specificity

Table 4. Binary Univariate Logistic Regression Results for Factors Affecting the Probability of Having a SIPD

	β	SE	Wald Statistics	p	Exp(β)	95% C.I.for exp(β)	
						Lower	Upper
SAPS							
Hallucinations	-0.043	0.035	1.497	0.221	0.958	0.895	1.026
Delusions	0.012	0.029	0.177	0.674	1.012	0.956	1.071
Bizarre Behaviour	0.325	0.111	8.506	**0.004**	1.384	1.113	1.722
Positive Formal Thought Disorder	0.088	0.048	3.437	0.064	1.092	0.995	1.199
SAPS, Total	0.014	0.014	0.940	0.332	1.014	0.986	1.043
SANS							
Affective Flattening or Blunting	0.346	0.080	18.875	**<0.001**	1.413	1.209	1.651
Alogia	0.805	0.214	14.123	**<0.001**	2.236	1.470	3.403
Unwillingness-Apathy	1.994	0.647	9.486	**0.002**	7.344	2.065	26.118
Anhedonia-Asociality	0.536	0.130	16.948	**<0.001**	1.708	1.324	2.205
Attention	0.347	0.151	5.302	**0.021**	1.415	1.053	1.901
SANS, Total	0.125	0.029	18.067	**<0.001**	1.133	1.070	1.201
PSYRATS							
Auditory hallucinations	-0.006	0.020	0.085	0.770	0.994	0.956	1.034
Delusions	0.045	0.078	0.341	0.559	1.046	0.899	1.218
PSYRATS, Total	-0.006	0.018	0.128	0.721	0.994	0.960	1.029
RMET							
Positive Affect	0.070	0.185	0.143	0.706	1.072	0.746	1.541
Negative Affect	-0.525	0.168	9.726	**0.002**	0.592	0.426	0.823
Neutral Affect	-0.461	0.134	11.782	**0.001**	0.630	0.484	0.820
RMET, Total	-0.248	0.076	10.593	**0.001**	0.780	0.672	0.906

*Adjusted for age, marital status, education level , β: Regression coefficient, SE: Standard error of the regression coefficient, Exp (β): Odds ratio, CI: Confidence Interval, p<0.05 value was considered statistically significant.

Table 5. Multiple Logistic Regression Results for Factors Affecting the Probability of Having SIPD*

	p	Exp(β)	95% C.I.for exp(β)	
			Lower	Upper
Model-1				
Constant	0.035	0.001		
SAPS Bizarre Behaviour	<0.001	1.421	1.194	1.690
SANS Affective Flattening or Blunting	0.043	1.452	1.012	2.084
Model Summary: Hosmer and Lemeshow Goodness of fit χ^2=2.764; p=0.948, Nagelkerke R^2=0.767 Variables entered on step 1: SAPS Hallucinations, Bizarre Behaviour, Positive Formal Thought Disorder; SANS Affective Flattening or Blunting, Attention, RMET Negative Affect, Neutral Affect Elemination method: Backward Wald				
Model-2				
Constant	0.010	0.001		
SAPS Bizarre Behaviour	0.023	1.594	1.066	2.384
SANS Total	<0.001	1.146	1.068	1.230
Model Summary: Hosmer and Lemeshow Goodness of fit χ^2=2.600; p=0.957, Nagelkerke R^2=0.783 Variables entered on step 1: SAPS Hallucinations, Bizarre Behaviour, Positive Formal Thought Disorder; SANS Total, RMET Total Elemination method: Backward Wald				

*Adjusted for age, marital status, education level, β: Regression coefficient, SE: Standard error of the regression coefficient, Exp (β): Odds ratio, CI: Confidence Interval, p<۰.۰۵ value was considered statistically significant.

Table 6. Evaluation of Performance in Predicting SIPD with ROC Curve Analysis of Scale Scores

	Cut-off	AUC	95% CI for AUC	p value	Sens	Spec	PPV	NPV
SAPS								
Hallucinations	<17.0	0.772	0.669 - 0.855	<0.001	70.7	75.5	72.5	73.9
Bizarre Behaviour	<7.0	0.813	0.715 - 0.889	<0.001	78.1	71.1	71.1	78.0
Positive Formal Thought Disorder	<6.0	0.786	0.684 - 0.867	<0.001	73.1	71.1	69.8	74.4
SANS								
Affective Flattening or Blunting	<4.0	0.944	0.872 - 0.982	<0.001	97.5	82.2	83.3	97.4
Alogia	<6.0	0.964	0.899 - 0.992	<0.001	97.5	86.6	87.0	97.5
Unwillingness-Apathy	<10.0	0.987	0.934 - 1.000	<0.001	100.0	88.8	89.1	100.0
Anhedonia-Asociality	<8.0	0.934	0.859 - 0.976	<0.001	95.1	84.4	84.8	95.0
Attention	<0.0	0.792	0.691 - 0.872	<0.001	73.1	73.3	71.4	75.0
Total	<43.0	0.943	0.870 - 0.981	<0.001	97.5	80.0	81.6	97.3
RMET								
Negative Affect	>4.0	0.824	0.727 - 0.898	<0.001	75.6	80.0	77.5	78.3
Neutral Affect	>17.0	0.849	0.755 - 0.917	<0.001	63.4	93.3	89.7	73.7
Total	>23.0	0.840	0.746 - 0.910	<0.001	63.4	88.8	83.9	72.7

AUC: Area under the curve; CI: Confidence Interval, Sens: Sensitivity, Spec: Specificity, PPV: Positive predictive value, NPV: Negative predictive value

was 71.1%. For SANS Blunted or Flattened Affect, the AUC value was 0.944, the optimum cut-off point was <4.0, sensitivity was 97.5%, and specificity was 82.2%. For SANS Total, the AUC value was 0.943, the optimum cut-off point was <43.0, sensitivity was 97.5%, and specificity was 80.0%. For SANS Diminished Energy and Interest, the AUC value was 0.987, the optimum cut-off point was <10.0, sensitivity was 100.0%, and specificity was 88.8% (Table-6) (Figure 1).

DISCUSSION

In our study, positive symptoms such as hallucinations and delusions, including their dimensional features, were evaluated in patients diagnosed with SIPD and schizophrenia patients without substance use. These features were compared between the two conditions, and differences in positive symptoms that could not be identified based on clinical observations were explored. Additionally, differences between psychotic symptoms and ToM abilities were examined in both groups, and the relationship between ToM abilities and psychotic symptoms was investigated. The aim was to identify clinical indicators that could assist in distinguishing between the two disorders.

Evaluation of Psychotic Symptoms

When examining the literature, it is apparent that there is still a lack of clarity regarding the differences between SIPD clinic and primary psychotic disorder clinic (McKetin et al. 2017; Inchausti et al. 2022). In a systematic review conducted by Wilson et al. six studies that met the inclusion criteria were included in a meta-analysis to investigate the clinical differences between SIPD and primary psychotic disorder. According to the findings of this meta-analysis, consistent clinical differences between the two patient groups were not reported (Wilson et al. 2018). However, while there is more consensus regarding differences in negative symptoms between primary psychotic disorder and SIPD, there is less consistency regarding differences in positive symptoms (Compton et al. 2004; Weibell et al. 2013). The lack of consensus in the literature regarding positive symptoms in SIPD can be attributed to several reasons. For example, in SIPD, positive symptoms tend to decline within a short period, and the timing of patient recruitment can greatly influence the results related to positive symptoms. In a study conducted by Dawe et al. it was noted that patients diagnosed with SIPD had similar levels of positive symptoms as those with primary psychotic disorders at the time of hospital admission, but these positive symptoms rapidly declined afterward. Consistent with our study findings, this study also emphasized that individuals diagnosed with SIPD had fewer negative symptoms compared to those diagnosed with primary psychotic disorders (Dawe et al. 2011).

In a study comparing psychotic symptoms between MA Induced Psychotic Disorder and schizophrenia patients, it was found that the total scores of SANS and the sub-scales of Blunted Affect and Alogia were significantly lower in MA Induced Psychotic Disorder patients compared to schizophrenia patients (Tomiyama, 1990). Our study also found that SANS total scores and scores of all sub-scales were higher in the SIPD group, and as scores on the Blunted Affect

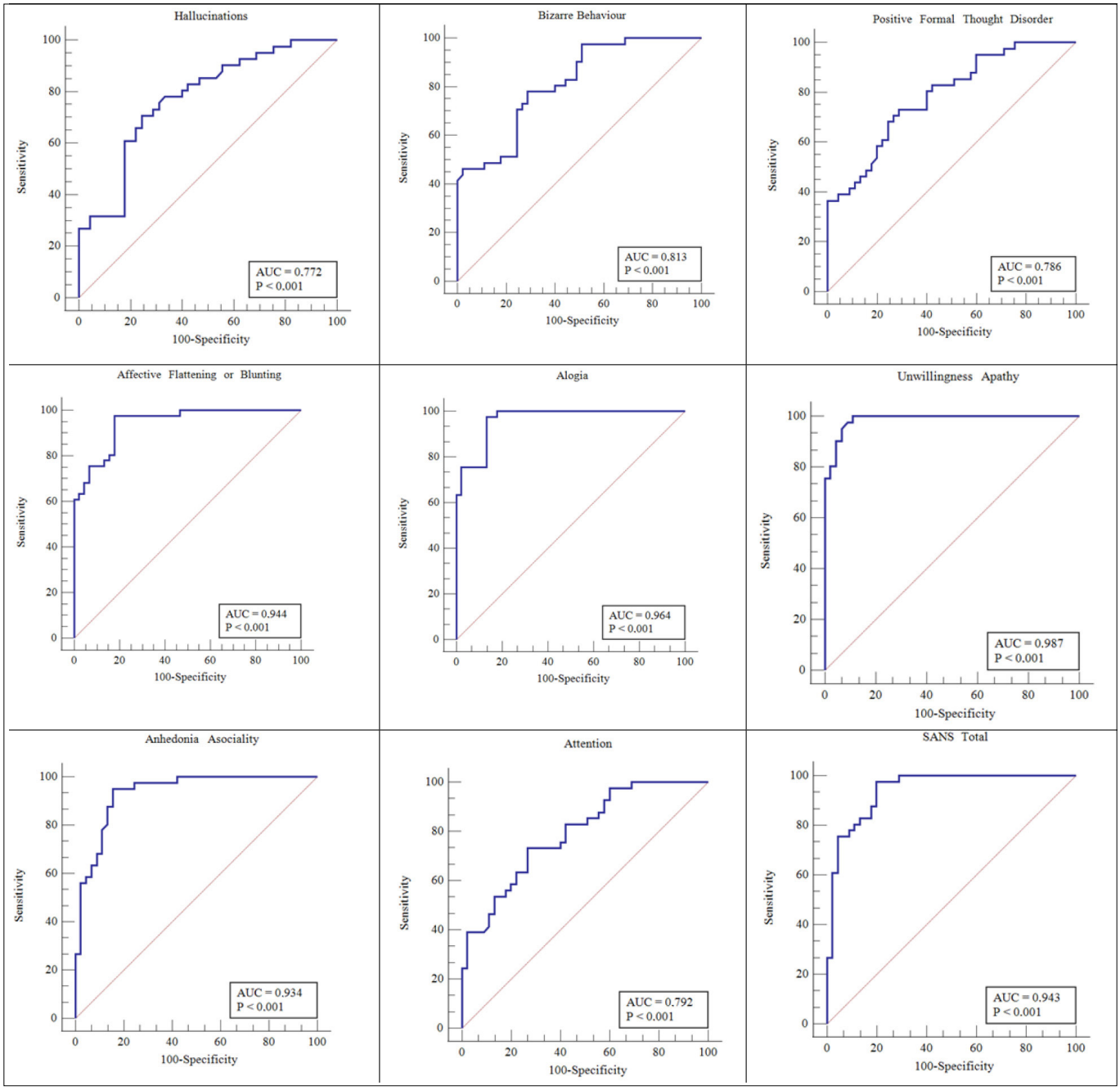

Figure 1. ROC Curve Analysis of Scale Scores of Performance in Predicting SIPD

sub-scale decreased, the risk of having SIPD increased, which is consistent with the findings of that study.

In an observational case-control study involving 238 patients that aimed to investigate the differences between SIPDs and non-SIPDs, individuals in the SIPD group scored significantly higher on positive symptoms, while those with non-SIPDs had higher scores on negative symptoms and severity (Cambra et al. 2023). The higher scores on negative symptom measures in patients with non-SIPDs are consistent with our study. However, it should be noted that our study differs in terms of finding higher positive symptom scores in individuals diagnosed with SIPD, which could be attributed to the evaluation of positive symptoms using the PANSS scale and the inclusion of patients using opioids and alcohol in the study.

In an epidemiological cohort study that included 544 cases diagnosed with first-episode psychosis, no significant difference was found in terms of positive psychotic symptoms measured by the SAPS between patients diagnosed with SIPDs and those with non-SIPDs (O'Connell et al. 2019). The lack of differences in delusion and hallucination scores and total scores measured by the SAPS is consistent with the findings of our study. However, in our study, patients with schizophrenia had higher scores on the positive formal thought and bizarre behavior subscales. The inclusion of patients with recurrent

episodes in our study was considered a possible reason for this difference. Another study investigating the differential diagnosis between SIPD and schizophrenia also found, in line with our study, that formal thought disorder and bizarre behavior were more prominent in schizophrenia (Rosenthal and Miner, 1997). Variations in the timing of the assessment of SIPD cases, methodological approaches, sample sizes, types of substances used, frequency and quantity of substance use, are seen to be associated with differing results in studies (Dawe et al. 2011). A study conducted in our country compared patients diagnosed with SC induced psychotic disorders and schizophrenia. In this study, consistent with the findings of our research, negative symptoms were found to be lower in psychotic disorders triggered by SC compared to schizophrenia patients, while positive symptoms were similar in both groups (Altintas et al. 2016). The similarity in the profiles of included patients and the high rate of SC use in our study (32 patients used SC, accounting for 74.4%) could explain this similarity. The absence of differences in both SAPS and PSYRATS scale scores for delusions and hallucinations in our study suggests the difficulty in distinguishing between these disorders based solely on delusions and hallucinations.

Evaluation of RMET

In our study, patients diagnosed with SIPD performed better on the RMET compared to patients diagnosed with schizophrenia. Patients with SIPD showed better recognition of negative and neutral eye expressions compared to patients with schizophrenia, and as their recognition performance of negative expressions and neutral expressions increased, the risk of having SIPD also increased. The performance in recognizing positive eye expressions was similar between both groups. While there are numerous studies in the literature investigating the relationship between substance use and ToM impairments or ToM deficits in schizophrenia, studies examining ToM performance in patients with SIPD are limited (Sanvicente-Vieira et al. 2017; Anne et al. 2018). It is still debated whether the ToM impairments in individuals with SIPD are caused by substance use itself or by the psychotic symptoms it induces (Ay et al. 2016). In a study comparing patients with MA-induced psychotic disorders, MA users, and healthy controls, both groups of MA users showed lower performance on the RMET compared to healthy controls, and the decline in performance was greater in MA-induced psychotic disorders compared to participants with MA use disorder (Anne et al. 2018). Similarly, in another study comparing MA users with and without psychotic symptoms and healthy controls in terms of ToM abilities, greater impairments in ToM were found in MA-induced psychotic disorders, but both groups of MA users showed worse emotion recognition abilities compared to healthy controls (Arunogiri et al. 2019). Furthermore, the causal direction of these relationships has not been determined. To clarify the nature of these longitudinal associations and obtain definitive results, future research with reduced confounding factors and larger samples is needed.

Limitations

One of the limitations of our study is related to the method of sample selection. The information regarding patients' substance use was based on their self-report, statements from their relatives, and medical records without supporting laboratory tests. The fact that patients may not provide accurate information about their substance use and that their relatives may not have sufficient knowledge can be considered as a limitation that restricts reliable data. Furthermore, in this study, the cases were evaluated at an average of 72 hours after their hospitalization. During this period, they were under medication, and different antipsychotic drugs were used. Another limitation of our study is that the ToM abilities of the included cases were evaluated solely using RMET. Additionally, the SIPD cases had varying variables such as the frequency of substance use, route of administration, and dosage, which are the limitations of our study. Furthermore, the potential impact of differences in the duration of psychotic disorders between the groups was not assessed, which is another limitation of our study.

CONCLUSIONS

SIPD diagnosed patients have fewer disorganized and negative symptoms (symptoms of behavioral and thought disorder) compared to patients diagnosed with schizophrenia. There is no difference between the two groups in terms of the severity, content, and dimensional features of delusions and hallucinations. Therefore, it does not seem possible to make a differential diagnosis between the two disorders based on positive symptoms. While SIPD diagnosed patients show better performance in recognizing negative and neutral expressions compared to schizophrenia diagnosed patients, their performance in recognizing positive expressions is similar in both groups. When making a differential diagnosis between SIPD and schizophrenia, the risk of being diagnosed with SIPD increases as blunting of affect, total negative symptoms, and odd behaviors decrease.

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