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Empirical redefinition of delusional disorder and its phenomenology: the DELIREMP study

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Abstract

Aims: Since Kraepelin, the controversy has persisted surrounding the nature of delusional disorder (DD) as a separate nosological entity or its clinical subtypes. Nevertheless, there has been no systematic study of its psychopathological structure based on patient interviews. Our goal was to empirically explore syndromic subentities in DD.
Methods: A cross-sectional study was conducted in 86 outpatients with DSM-IV-confirmed DD using SCID-I. Psychopathological factors were identified by factor analysis of PANSS scores. The association between these factors and clinical variables (as per standardized instruments) was analyzed using uni- and multivariate techniques.
Results: PANSS symptoms were consistent with four factors (*Paranoid, Cognitive, Schizoid*, and *Affective* dimensions), accounting for 59.4% of the total variance. The *Paranoid Dimension* was associated with premorbid paranoid personality disorder, more adverse childhood experiences, chronic course, legal problems, worse global functioning, and poorer treatment adherence and response. The *Cognitive Dimension* was associated with poorer cognitive functioning, premorbid substance abuse, comorbid somatic diseases, mainly non-prominent visual hallucinations, fewer comorbid depressive disorders, and poorer global functioning. The *Schizoid Dimension* was associated with being single, a family history of schizophrenia, premorbid personality disorders (largely schizoid and schizotypal), non-prominent auditory hallucinations, and dysthymia. Finally, the *Affective Dimension* was associated with a family history of depression, premorbid obsessive personality, somatic delusions, absence of reference delusions, tactile and olfactory hallucinations, depressive and anxiety disorders, risk of suicide, and higher perceived stress.
Conclusion: The identification and clinical validation of four separate psychopathological dimensions in DD provide evidence toward a more accurate conceptualization of DD and its types.

1. Introduction

The psychopathology and nosology of paranoia/delusional disorder (DD) have been the objects of discussion since the time of Kraepelin [1], who defined paranoia as a chronic delusional condition where no deterioration or hallucinations occur, unlike *dementia praecox* (schizophrenia). By contrast, Bleuler [2] classified paranoia as a rare form of schizophrenia in which hallucinations may sometimes occur. Kleist [3] believed paranoia to result from a mood disorder, whereas Krueger [4] considered it to be a congenital affective derangement. Kretschmer [5] reported a type of paranoia, *sensitive delusion of reference*, which is triggered in the setting of a premorbid personality (sensitive people with depressive, pessimistic, and narcissistic traits), adverse life events and social circumstances, and no progression to schizophrenia. Henderson and Gillespie [6] subsequently described the concept of the *paranoid spectrum*, which

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includes paranoia, paraphrenia, and paranoid schizophrenia. Along the same lines, Schneider [7] contemplated paranoia as a peripheral type of schizophrenic psychosis. After decades with virtually no scientific interest in paranoia, the nosological controversy surrounding DD has recently resurfaced as a result of paranoia being alternatively considered a subtype of schizophrenia [8], a subtype of mood disorders [9], a separate homogeneous nosological entity [10], and a specific group of nosological entities [11].

There is a paucity of empirical studies of DD available and the ones that do exist use different diagnostic criteria. They are also based on small sample sizes and are usually poorly systematized. Nevertheless, in 1987, the American classification of mental disorders reintroduced the Kraepelinian concept of paranoia as a separate nosological entity within psychotic disorders in the DSM-III-R [12], which was later consolidated in DSM-IV under the term "delusional disorder" as a clearly distinct entity different from schizophrenia which has to be completely ruled out before making a diagnosis of DD [13]. Validation of a diagnosis of DD is based fundamentally on sociodemographic, family, and diagnostic stability studies [11]. Age at onset is older than in schizophrenia and gender distribution differs from that of affective disorders, which predominate in women [14]. Most family studies have not shown a higher incidence of schizophrenia or mood disorders in the relatives of patients with DD [15–20]. Follow-up studies reveal that DD is rediagnosed as schizophrenia in 3%–28% of patients and as mood disorders in 3%–8%, while all other DD diagnoses remain stable [21]. In contrast, biological, psychopathological, and family studies questioning the diagnostic independence of DD from schizophrenia and affective disorders have appeared in recent years. Neurophysiological [22,23], neuropsychological [24], and genetic [25] studies have compared DD with schizophrenia and failed to detect any significant differences. Insofar as affective disorders are concerned, several studies have evidenced large subsamples of patients with DD and comorbid depression (43%–54%) [26–29] and one study found that cases of DD with depression presented a significantly more pervasive family history of affective disorders than did cases without depression [29]. Furthermore, the significance of subtle cerebral organic factors in DD has also been described, such as prior brain damage and premorbid substance abuse or onset at an advanced age (aging) [30–32].

The relevance of considering a cognitive dimension in DD has been supported by several studies [33,34]. These studies share a neuroscience approach to psychopathology [35], and include the use of neuroimaging techniques, genetic testing or cognitive neuropsychology. Following this perspective, we pose that within DD there are a variety of psychopathological dimensions including one comprising cognitive deficits as reviewed recently [36–38]. We set to test whether such a cognitive dimension empirically emerges from DD patients' phenomenology and, should that be the case, to validate it against a variety of expected clinical correlates such as educational level or performance on cognitive impairment tests.

According to DSM-IV, the main diagnostic criterion for DD, based on Kraepelin's concept of paranoia [39], is the presence of a non-bizarre delusion for longer than one month. However, DD symptoms are markedly polymorphic, as follows: (1) the content, intensity, and degree of insight of the delusions can vary substantially [40–42]; (2) the association with paranoid symptoms such as suspiciousness, excitation, hostility, motor tension, and grandiosity are very frequent [31,43]; (3) approximately half of the patients have a depressive syndrome [26–29]; (4) at least one fifth of all patients experience tactile and olfactory hallucinations or other types of hallucinations if these are non-prominent and are consistent with delusional subject matter [27,44]; (5) symptoms of schizoid and schizotypal personality are not uncommon [45–47], and (6) there is evidence of mild cognitive impairment [48–50] and lower IQ [51] than in the healthy population, possibly due to very subtle organic brain factors. Despite the heterogeneity of symptoms in DD, the DSM-IV classification of DD into seven types is based solely on the predominant theme of the delusional idea [13]. It is striking that DSM-IV supports such a content-based classification unfounded on studies that assess the symptomatic structure and that validate it nosologically.

Despite the clinical significance of DD and the fact that it is more prevalent than previously thought [52], it continues to be poorly understood and understudied. Further empirical research into complex DD symptoms should be performed to discern its true symptom structure and the validity of its current subtypes. Surprisingly, only the study by Serreti et al. [53] provides a factor analysis of the psychopathology of DD. This study retrospectively assessed the lifetime symptoms of 108 patients admitted to hospital with a diagnosis of DD (DSM-III-R criteria) using an operational criteria checklist for psychotic illness (OPCRIT) rather than direct interviewing of DD patients. Delusional symptoms were found to be limited to four independent factors: (I) core depressive symptoms, (II) hallucinations, (III) delusions, and (IV) irritability. This suggests substantial heterogeneity in the diagnostic category of DD. The primary aim of our study was to empirically explore syndromic subentities in DD under the hypothesis that there might be a better way to classify DD other than the content of the delusions, i.e. there may be an underlying psychopathological structure that could provide symptom dimensions expressed to different degree across different DD patients. To this end, the PANSS was used to identify symptom dimensions; the validity of these symptom dimensions was then tested on the basis of how they relate to other symptom scales and instruments, as well as by modelling their associations with sociodemographic characteristics, potential risk factors, clinical correlates, functionality, and treatment response.

2. Methods

2.1. Subjects

A cross-sectional sample of 106 individuals with a diagnosis of DD was randomly selected from a computerized

case register [44] of 5 Community Mental Health Centers (CMHCs) belonging to Sant Joan de Déu-Mental Health Services (SJD-MHS). SJD-MHS is a state-funded institution providing comprehensive psychiatric care through both community and hospital facilities and serving a population of some six-hundred thousand inhabitants in a well-defined area of southern Barcelona, Spain. The inclusion criteria were: (a) a primary diagnosis of DD (according to DSM-IV criteria); (b) age over 18 years; (c) residence in the catchment areas of the participating CMHCs; (d) at least 1 outpatient visit during the 6 months preceding the beginning of the study; (e) referring psychiatrist's approval to participate in the study, and (f) patient agreement to participate. The exclusion criteria were: (a) diagnosis of mental retardation; (b) unconfirmed diagnosis of DD using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (psychosis module) [54,55]. Of the initial 106 individuals selected from the database, 6 patients refused to participate in the study, 8 patients did not receive the approval of their referring psychiatrist, and 6 patients did not have a SCID-I-confirmed diagnosis of DD (3 fulfilled the criteria for schizophrenia, 1 for schizoaffective disorder, 1 for psychotic disorder due to a general medical condition, and 1 for substance-induced psychotic disorder). Eighty-six patients were included in the study and completed the evaluation, thereby comprising the final study sample (n = 86). All patients were evaluated by a postgraduate psychology student formally trained to use all the study instruments. All patients were provided with a complete description of the study and gave their written informed consent to participate after they had been invited to do so in a letter from their psychiatrist. The study was approved by the Ethics Committee of the SJD-MHS.

2.2. Variables and instruments

2.2.1. Diagnosis of DD

The diagnosis of DD was validated using the psychosis module of the Structured Clinical Interview for DSM-IV axis I disorder, clinical version (SCID-I CV) [54,55]. Patients were assigned to one of seven DD DSM-IV types (persecutory, jealous, somatic, erotomaniac, grandiose, mixed, and not otherwise specified).

2.2.2. Sociodemographic and Potential Risk Factors for DD

A systematic inventory, described in greater detail elsewhere [56], was used to record demographic variables (age, sex, educational level, marital status, living with others). The presence of adverse childhood experiences (ACEs) was evaluated with questions adapted from the Conflict Tactics Scale (CTS) [57]. This questionnaire covers three categories of childhood abuse (emotional abuse [two questions], physical abuse [two questions], and physical contact sexual abuse [four questions according to Wyatt]) [58], and five categories of exposure to household dysfunction during childhood (exposure to substance abuse [two questions] [59], mental illness [two questions], violent treatment of mother or stepmother [four questions] [57], criminal behavior in the household [one question], and parental separation or divorce [one question]). Respondents were defined as exposed to a category if they responded "yes" to one or more of the questions in that category. All questions regarding ACEs referred to the respondents' first 18 years of life and have been described in detail elsewhere [60]. The Standardized Assessment of Personality (SAP) [61,62] was used to assess premorbid personality. The SAP is adapted to the DSM-IV diagnostic criteria for personality disorders and detects both the presence and type of personality disorder – regardless of the nature of the disease – using a short, semi-structured interview with a respondent (relative or close friend). The systematic inventory was also used to record other variables of potential risk factors such as family history of mental disorders in first- and second-degree relatives, premorbid deafness (defined as hearing loss leading to communication difficulties), premorbid immigration, premorbid head trauma with loss of consciousness, premorbid substance abuse (according to DSM-IV criteria), somatic illnesses according to DSM-IV axis III, and precipitating factors according to axis IV of DSM-IV.

2.2.3. Psychopathology, Axis I Comorbidity and Course

All the clinical instruments included in this section are not self-administered measures but rather need to be administered by accordingly trained clinicians. Psychotic psychopathology was assessed using the PANSS [63,64] and a history of psychotic psychopathology was examined using Module B (psychotic and associated symptoms) of SCID-I CV [54,55]. The severity of depressive symptoms was evaluated using the Montgomery–Asberg Depression Rating Scale (MADRS) [65,66]. Global cognitive functioning was evaluated using the Mini Mental State Examination, 30-item version (MMSE-30) [67,68]. Co-existing DSM-IV axis I psychiatric disorders and risk of suicide were diagnosed using the Mini International Neuropsychiatric Interview (MINI) for DSM-IV [69,70]. Other clinical variables were also collected following a systematic inventory: attempted suicide, problems with the law because of violent behavior, age at onset of DD, age at first psychiatric consultation, form of onset (acute [<3 months] or insidious [>3 months]), time since onset, and course of illness (uninterrupted chronic or phasic with total remission).

2.2.4. Functionality and Treatment of DD

Global functioning was assessed using the Global Assessment of Functioning (GAF) scale [13] and disability was measured using the Sheehan Disability Inventory (SDI) [70,71]. The SDI consists of five items grouped into three scales: (1) disability, comprised of the first three items and assessing the extent to which symptoms interfere with three domains of the patient's life (work, social life, and family life); (2) perceived stress, which appraises the degree to which stressful events and personal problems have affected the patient's life, and (3) social support, which gauges the

support received by the patient as compared to the support needed. The first four items are scored on a Likert scale from 0 (none at all) to 10 (extremely). The fifth item is scored on a percentage scale, where 100% means that patients receive all the support they need. Thus, three scores are obtained, one for each scale. The disability score is calculated by adding the scores from each of the three scale items. The systematic inventory was also used to record utilization of psychiatric resources (number of lifetime psychiatric admissions and visits to the emergency room in the last five years) and taking of antipsychotic treatment. Treatment adherence was evaluated using the Bäuml Treatment Adherence Scale (BTAS) [72], which consists of a single item that assesses treatment compliance using a four-point Likert scale ranging from 1 (very good) to 4 (poor). A retrospective assessment of any global improvement on the condition resulting from any previous therapeutic interventions was assessed using the rater-administered Clinical Global Impression-Global Improvement (CGI-GI) Scale [73]. The scale consists of a single item that examines change using a 5-point Likert scale ranging from 0 (worse) to 4 (better).

2.3. Statistics

2.3.1. Factor Analysis

The following steps were used for variable reduction in line with the parsimony principle: (1) symptoms absent in more than 80% of the cases were removed to avoid strongly biased variables; (2) the correlation matrix with all variables was calculated and variables shown to be less correlated were eliminated; (3) variables not accounting for more than 0.4 of total variance (communality) and variables with a low factor load (r <0.4) were deleted, and (4) after deciding on an analysis of four factors that were clinically interpretable and had eigenvalues of greater than one, a varimax rotation was performed to simplify the interpretation of the structure obtained in the loading matrix [74]. Finally, sixteen of the 30 PANSS items conformed the factor analysis (Principal Component Method, PCM). The model was then validated based on the following criteria: (1) the ratio between the number of variables and the number of observations (patients) should not exceed 1:5 [75]; (2) a Bartlett sphericity test to check model suitability, and (3) the Kaiser–Meyer–Olkin (KMO) measure of sample adequacy.

2.3.2. Association between Psychopathological Factors and Clinical Variables

Differences between the scores for psychopathological factors and sociodemographic and clinical qualitative variables were measured using nonparametric Mann–Whitney U tests for two independent samples and Kruskal–Wallis tests for k independent samples. Differences between scores for factors and quantitative variables were determined using Pearson's correlation analysis. Some variables had fewer than six cases presenting the sociodemographic or clinical condition in question, and, as a result, were not included in those bivariate analyses, given that the test requires more subjects in order to assure adequate test power for multiple comparisons [76,77]. A multivariate analysis (linear regression models) was performed to determine which sociodemographic and clinical variables are associated with each of the four psychopathological factors. The variables included in the linear regression model were those bivariately associated with any of the psychopathological factors with a confidence level of 0.10; but the reduction of the model was conducted using a stepwise method, with a type I error of 0.0.05. Multicollinearity was controlled for using a condition index of less than 20 and the hypothesis of normality and randomness for the residuals was determined using the Lilliefors and runs test for each model, both with a confidence level of 0.05.

3. Results

3.1. Sociodemographic and clinical characteristics of the sample

Complete data for all patients were included in the analysis. The sample's characteristics have been detailed at length elsewhere [56]. In short, the patients' mean age was 54.0 years (SD = 14.4) and women accounted for 61.6% of the total sample. Marital status was the most frequent married (52.3 %), followed by single (24.3%), the separated / divorced (16.3%) and widowed (7.0%). 61.6% of the sample reports a psychiatric family history, including affective disorders (25.6%), schizophrenia (20.6%) and delusional disorder (17.4%). Sixty-four percent had a premorbid personality disorder, the most common being paranoid (38.4%), followed by schizoid (12.8%), obsessive (11.6%), avoidant (9.3%), schizotypal (8.1%), dependent (5.8%), narcissistic (4.7%), borderline (2.3%), and histrionic (2.3%). There was not any patient with antisocial disorder reported. The persecutory DD subtype was the most common presentation (59.3%), followed by the jealous subtype (22.1%), erotomaniac (4.7%), grandiose (4.7%), somatic (59.3%) and mixed (5.8%). Mean scores on the positive and negative PANSS subscales were 13.8 (SD = 4.5) and 9.9 (SD = 2.8), respectively, and the mean general symptom score (PANSS) was 23.8 (SD = 4.8). Affective disorders were found in 32.6%, with depressive disorder in 16.3% of the sample, and dysthymia in 17.4%. Anxiety disorders, eating disorders and substances abuse were found in 14.0%, 1.2%, and 4.7% of patients, respectively. Regarding SDI, disability score about a mean = 13.8 (SD = 7.8) [*work/school*, mean = 5.2 (SD 3.5); *social life,* mean = 4.3 (SD 2.9); and *family,* mean = 4.2 (SD 2.1)]. Table 1 presents the sociodemographic and clinical characteristics of the study sample.

3.2. Psychopathological dimensions of DD

The PCM factor analysis using PANSS symptoms extracted a four-factor structure accounting for 59.4% of total variance. The Barlett's sphericity test proved model adequacy (p = 0.000), while a KMO measure of 0.62 demonstrated sample adequacy. Table 2 summarizes the factors (psychopathological

Table 1
Sample description.

Socio-demographic and Potential Risk Factors		Delusion types (SCID-I)	
Age, years	54.0 (SD 14.4)	Delusions of reference	65 (75.6%)
Sex		Persecutory delusions	71 (82.6%)
Men	33 (38.4%)	Grandiose delusions	6 (7.0%)
Women	53 (61.6%)	Somatic delusions	10 (11.6%)
Years in education	7.3 (SD 5.1)	Jealous delusions	27 (31.4%)
Living with others		Erotomamiac delusion	9 (10.5%)
No	17 (19.8%)	Hallucinations (SCID-I)	39 (45.3%)
Yes	69 (80.2%)	Non-prominent auditory	13 (15.1%)
Psychiatric family history	53 (61.6%)	Non-prominent visual	7 (8.1%)
Number of ACEs	2.7 (SD 1.8)	Tactile	18 (20.9%)
Premorbid personality disorder (SAP)	54 (64.0%)	Olfactory	14 (16.3%)
Premorbid isolation	17 (19.8%)	Non-prominent gustatory	4 (4.7%)
Premorbid immigration	8 (9.3%)	No. of suicide attempts	0.29 (SD 0.7)
Premorbid deafness	16 (18.6%)	Legal problems	24 (27.9%)
Precipitating factors	41 (47.7%)	Depression Score (MADRS)	7.8 (SD 7.3)
Premorbid substance abuse	16 (18.6%)	Cognitive function Score (MSEE-30)	27.6 (SD 2.4)
Premorbid head trauma	15 (17.4%)	Comorbidity in axis I (MINI)	40 (46.5%)
Onset at an older age (>50 years)	21 (24.4%)		
Somatic illnesses	37 (43.0%)	Functionality and Treatment	
		Global functioning score (GAF)	63.9 (SD 11.3)
Clinical Variables		Total disability score (SDI)	13.8 (SD 7.8)
Age at onset, yrs	39.6 (SD 14.5)	Perceived stress score (SDI)	2.3 (SD 2.9)
Age at first consultation, yrs	43.4 (SD 14.9)	Social support score (SDI)	69.3 (SD 33.4)
Years since diagnosis	14.6 (SD 12.2)	Psychiatric admission	42 (48.8%)
Type of onset		No. of psychiatric admissions	0.9 (SD 1.3)
Acute	25 (29.1%)	No. of visits to the emergency room	1.5 (SD 3.0)
Insidious	61 (70.9%)	Antipsychotic treatment	78 (90.7%)
Type of course		Treatment adherence (BTAS)	1.6 (SD 0.9)
Chronic	78 (91.7%)	Treatment response (CGI-GI)	1.8 (SD 0.9)
Phasic	8 (9.3%)		

Abbreviations: ACEs, adverse childhood experiences; PD, personality disorder; SAP, Standard Assessment of Personality; SCID-I, Structured Clinical Interview for DSM-IV Axis I Disorders; MADRS, Montgomery–Asberg Depression Rating Scale; MMSE-30, Mini Mental State Examination, 30-item version; MINI, Mini International Neuropsychiatric Interview; GAF, Global Assessment of Functioning; SDS, Sheehan Disability Scale; BTAS, Bäuml Treatment Adherence Scale; CGI-GI, Clinical Global Impression Scale-Global Improvement.

Table 2
Factorial analysis of the PANSS.

PANSS	Communality	FACTOR I	FACTOR II	FACTOR III	FACTOR IV
		Paranoid Dimension	Cognitive Dimension	Schizoid Dimension	Affective Dimension
Delusions (P1)	.624	.734			
Excitation (P4)	.602	.722			
Lack of judgment (G12)	.663	.686			
Suspiciousness (P6)	.470	.660			
Hostility (P7)	.507	.637			
Conceptual disorganization (P2)	.761		.864		
Decreased speech fluidity (N6)	595		.734		
Motor retardation (PG7)	.543		.680		
Difficulty for abstract thinking (N5)	.604		.612		
Emotional coldness (N2)	.752			.842	
Social withdrawal (G16)	.679			.812	
Unusual thought contents (G9)	.640			.705	
Feelings of guilt (G3)	.600				.759
Somatic concern (G1)	.524				.711
Anxiety (G2)	.525				.650
Depression (G6)	.421				.535
Explained variance (cumulative %)		21.3	36.2	48.2	59.4
Eigenvalues		3.4	2.4	1.9	1.8

Table 3
Relationships between psychopathological dimensions and sociodemographic and potential risk factors, clinical aspects, functionality, and treatment with a maximum confidence level of 0.10.

		PARANOID		COGNITIVE		SCHIZOID		AFFECTIVE	
		Rank/Statistic		Rank/Statistic		Rank/Statistic		Rank/Statistic	
Socio-demographic and potential risk factors									
Marital status		KW = 1.36		KW = 5.74		KW = 15.56***		KW = 6.31*	
Years in education		r = −0.02		r = −0.257**		r = 0.16		r = 0.03	
Living with others	Yes	54.00	U = 408*	49.18	U = 490	52.35	U = 436	32.71	U = 403**
	No	40.91		42.10		41.32		46.16	
Psychiatric family history	Yes	41.47	U = 767	39.11	U = 642**	43.36	U = 867	44.58	U = 817
	No	46.76		50.55		43.73		41.76	
Schizophrenia	Yes	43.53	U = 610	44.17	U = 600	54.78	U = 409**	40.56	U = 559
	No	43.39		43.32		40.51		44.28	
Delusional disorder	Yes	38.93	U = 464	31.67	U = 355**	38.47	U = 457	40.47	U = 487
	No	44.46		46.00		44.56		44.14	
Affective disorder	Yes	43.09	U = 695	33.64	U = 487**	40.68	U = 642	54.41	U = 464**
	No	43.68		46.89		44.47		39.75	
Number of ACES		r = 0.21*		r = −0.20*		r = 0.05		r = 0.05	
Premorbid personality (SAP)	Yes	45.43	U = 760	44.69	U = 800	48.87	U = 574***	47.96	U = 623**
	No	40.25		41.50		34.44		35.97	
Paranoid PD	Yes	48.33	U = 715*	42.94	U = 856	47.88	U = 730	45.55	U = 807
	No	40.49		43.85		40.77		42.23	
Schizoid PD	Yes	37.18	U = 343	54.91	U = 287	64.45	U = 182***	46.73	U = 377
	No	44.43		41.83		40.43		43.03	
Schizotypal PD	Yes	56.86	U = 183	52.14	U = 216	68.86	U = 99***	44.14	U = 272
	No	42.32		42.73		41.25		43.44	
Obsessive PD	Yes	42.40	U = 369	30.20	U = 247*	30.20	U = 267	62.10	U = 194**
	No	43.63		45.25		44.99		41.05	
Premorbid isolation	Yes	54.00	U = 408*	49.18	U = 490	52.35	U = 436	32.71	U = 403**
	No	40.91		42.10		41.32		46.16	
Precipitating factors	Yes	40.07	U = 782*	44.02	U = 901	44.20	U = 894	40.34	U = 793
	No	46.62		43.02		42.87		46.38	
Premorbid substance abuse	Yes	33.63	U = 402*	55.00	U = 376**	44.31	U = 547	49.69	U = 461
	No	45.76		40.87		43.31		42.09	
Onset at an older age (> 50 years)	Yes	44.33	U = 665	52.81	U = 487**	36.29	U = 531	31.86	U = 438
	No	43.23		40.49		45.83		47.26	
Somatic illnesses	Yes	42.49	U = 869	49.73	U = 676**	36.57	U = 650**	43.73	U = 898
	No	44.27		38.80		48.73		43.33	
Clinical variables									
Somatic delusions(SCID-I)	Yes	42.40	U = 369	48.30	U = 332	36.00	U = 305	60.10	U = 214**
	No	43.64		42.87		44.49		41.32	
Delusions of reference (SCID-I)	Yes	41.85	U = 575	40.34	U = 477**	44.32	U = 860	34.00	U = 483**
	No	48.62		53.29		40.95		46.57	
Delusions of grandeur (SCID-I)	Yes	59.00	U = 147	54.67	U = 173	44.67	U = 233	17.83	U = 86**
	No	42.34		42.66		43.41		45.43	
Hallucinations (SCID-I)	Yes	44.85	U = 864	51.10	U = 620**	45.31	U = 846	48.90	U = 706*
	No	42.38		37.19		42.00		39.02	
Non-prominent auditory hallucinations	Yes	44.77	U = 458	53.54	U = 344	54.85	U = 327*	41.38	U = 447
	No	43.27		41.71		41.48		43.88	
Non-prominent visual hallucinations	Yes	29.14	U = 176	76.14	U = 48***	52.57	U = 213	38.57	U = 242
	No	44.77		40.61		42.70		43.94	
Tactile hallucinations	Yes	45.78	U = 571	47.61	U = 538	37.78	U = 509	54.94	U = 406**
	No	42.90		42.41		45.01		40.47	
Olfactory hallucinations	Yes	44.93	U = 484	51.36	U = 394	42.71	U = 493	56.29	U = 325**
	No	43.22		41.97		43.65		41.01	
No. of suicide attempts		r = 0.09		r = 0.02		r = −0.11		r = 0.60***	
Legal problems due to violence	Yes	57.96	U = 397***	45.29	U = 701	41.79	U = 703	39.08	U = 638
	No	37.90		42.81		44.16		45.21	
Jealous DD type (DSM-IV)	Yes	40.32	U = 576	34.00	U = 456*	45.21	U = 604	45.74	U = 594
	No	44.40		46.19		43.01		42.87	
Depression score (MADRS)		r = 0.00		r = 0.05		r = 0.20*		r = 0.36***	
Cognitive function score (MSEE)		r = 0.07		r = −0.46***		r = −0.07		r = 0.80	

Table 3 (*continued*)

		PARANOID		COGNITIVE		SCHIZOID		AFFECTIVE	
		Rank/Statistic		Rank/Statistic		Rank/Statistic		Rank/Statistic	
Comorbidity in axis I (MINI)	Yes	44.03	U = 899	39.67	U = 767	52.30	U = 568**	58.43	U = 323***
	No	43.04		46.83		35.85		30.52	
Depressive disorders	Yes	39.93	U = 712	33.20	U = 437***	53.54	U = 531***	61.32	U = 313***
	No	45.22		45.68		38.66		34.90	
Major depression	Yes	44.50	U = 490	24.86	U = 243***	47.57	U = 447	58.79	U = 290**
	No	43.21		47.13		42.71		40.53	
Dysthymia	Yes	45.59	U = 384*	49.97	U = 378*	60.40	U = 279***	62.80	U = 243***
	No	33.60		30.11		39.93		39.42	
Anxiety disorders	Yes	44.75	U = 429	54.17	U = 316	57.42	U = 277**	62.58	U = 215***
	No	43.30		41.77		41.24		40.41	
Suicide risk (MINI)	Yes	36.00	U = 377	44.69	U = 459	48.77	U = 406	63.38	U = 216***
	No	44.84		43.29		42.56		39.96	
Type of course	Yes	22.13	U = 141**	40.00	U = 284	58.63	U = 191*	48.38	U = 273
	No	45.69		43.86		41.95		43.00	
Functionality and treatment									
Social life (SDI)		r = 0.16*		r = 0.22**		r = 0.16		r = −0.30	
Perceived stress (SDI)		r = 0.12		r = 0.05		r = −0.06		r = 0.34***	
Social support (SDI)		r = −0.22**		r = 0.02		r = −0.04		r = 0.03	
Global functioning (GAF)		r = −0.48***		r = −0.52***		r = −0.15		r = −0.00	
No. of psychiatric admissions		r = −0.03		r = 0.24**		r = −0.10		r = 0.19*	
Antipsychotics	Yes	41.56	U = 161**	43.32	U = 298	44.55	U = 230	44.94	U = 200
	No	62.38		45.25		33.25		29.50	
Treatment adherence (BTAS)		r = 0.46 ***		r = 0.15		r = 0.09		r = −0.05	
Treatment response (CGI-GI)		r = 0.43***		r = 0.13		r = −0.02		r = 0.11	

(A): The dimension presents higher values of the median in the absence of the variable. (B): Being single presents higher values of the dimension. (C): Being married presents higher values of the dimension. (D): Chronic course presents higher values of the dimension. (E): Phasic course presents higher values of the dimension. Abbreviations: ACEs, Adverse Childhood Experiences; PD, personality disorder; SAP, Standard Assessment of Personality; SCID-I, Structured Clinical Interview for DSM-IV Axis I Disorders; MADRS, Montgomery–Asberg Depression Rating Scale; MMSE, Mini Mental State Examination, 30-item version; MINI, Mini International Neuropsychiatric Interview; GAF, Global Assessment of Functioning; SDS, Sheehan Disability Scale; BTAS, Bäuml Treatment Adherence Scale; CGI-GI, Clinical Global Impression Scale-Global Improvement. N.S., non-significant. U, Mann–Whitney U Test; KW, Kruskal–Wallis Test.

* $p < 0.10$.

** $p < 0.05$.

*** $p < 0.01$.

dimensions) extracted, their components, and their loading values. In brief, we named the *Paranoid Dimension* a factor clustering five typical paranoid symptoms (delusions, excitation, lack of judgment, suspiciousness, and hostility) with an eigenvalue of 3.4 and that accounts for 21.3% of the total variance. The *Cognitive Dimension* consists of four symptoms (conceptual disorganization, impaired fluency of speech, motor retardation, and impaired capacity for abstract thinking), has an eigenvalue of 2.4, and accounts for 14.9% of total variance. The *Schizoid Dimension*, with an eigenvalue of 1.9 and accounting for 12.1% of total variance is comprised of three schizoid and/or schizotypal symptoms (social withdrawal, emotional coldness, and unusual thought content). Finally, the *Affective Dimension* is made up of four symptoms of the anxious–depressive syndrome (feelings of guilt, somatic concern, anxiety, and depression), has an eigenvalue of 1.8, accounting for 11.1% of total variance.

3.3. External validation of psychopathological dimensions

Table 3 presents all bivariate associations with the four DD psychopathological dimensions. In summary, the *Paranoid Dimension* was bivariately associated with premorbid paranoid personality disorder ($p = 0.057$), the *Cognitive Dimension* with lower cognitive functioning ($r = -0.457$, $p = 0.000$), the *Schizoid Dimension* with premorbid schizoid and schizotypal personality disorders ($p = 0.003$ and $p = 0.005$, respectively), and finally, the *Affective Dimension* with greater severity of depression ($r = 0.359$, $p = 0.001$) and depressive and anxiety disorders ($p = 0.000$ and $p = 0.004$, respectively). We found no associations between the four psychopathological dimensions with DD or with delusion types, with the exception of the jealous type, associated with less intense cognitive symptoms ($p = 0.060$), and somatic delusions, associated more intense affective symptoms ($p = 0.025$).

Finally, a multiple regression analysis was used to determine multivariable independent associations with all four psychopathological dimensions. Fig. 1 summarizes the results of such regression models for each psychopathological dimension. In brief, the *Paranoid Dimension* is independently associated to legal problems due to violence, chronic course of disease, lower global functioning, and poorer adherence (adjusted $R^2 = 0.424$). The *Cognitive Dimension* was found to associate with comorbid somatic

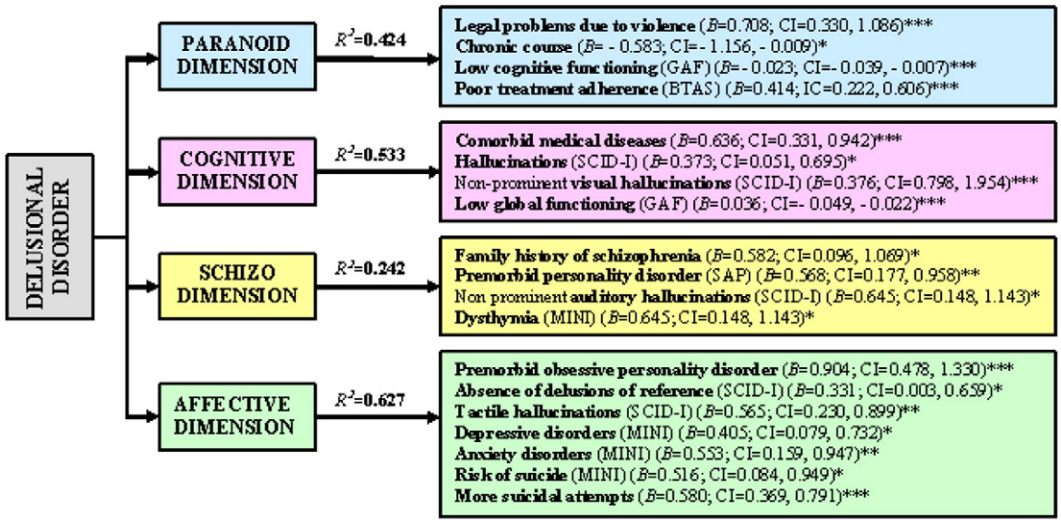

Fig. 1. Linear regression models for the psychopathological dimensions according to clinical variables (initial models include variables with maximum bivariate association of 0.10 and maximum significance value in the final model of 0.05). (*) $p < 0.05$; (**) $p < 0.01$; (***) $p < 0.001$. Abbreviations: SAP, Standard Assessment of Personality; SCID-I, Structured Clinical Interview for DSM-IV Axis I Disorders; Mini Mental State Examination, 30-item version; MINI, Mini International Neuropsychiatric Interview; GAF, Global Assessment of Functioning; BTAS, Bäuml Treatment Adherence Scale. *B*, coefficient of the variable; CI, confidence interval.

diseases, hallucinations in general (and no-prominent visual hallucinations in particular), and poorer global functioning (adjusted $R^2 = 0.533$). The *Schizoid Dimension* had had a multivariate association with a positive family history of schizophrenia, premorbid personality, non-prominent auditory hallucinations, and dysthymia (adjusted $R^2 = 0.242$). Finally, the *Affective Dimension* was independently associated to premorbid obsessive personality, more suicide attempts, absence of reference delusions, tactile hallucinations, depressive and anxiety disorders, and risk of suicide (adjusted $R^2 = 0.627$).

4. Discussion

This is the first study to empirically explore the symptom structure of DD using objectively-measured symptom scores obtained from direct clinical interviews with patients. The study sample is the largest DD sample explored to date using a standard structured interview for psychotic disorders. Our primary aim was to identify psychopathological dimensions in DD and to validate such dimensions by exploring their associations with a wide array of validly measured clinical features along with sociodemographic correlates and potential risk factors. Indeed, all four psychopathological dimensions identified (*Paranoid, Cognitive, Schizoid*, and *Affective*) associate independently with external clinical variables that are both congruently and coherently linked to symptoms in each dimension. Given that previous knowledge regarding DD construct validity was mainly based on classical descriptions, we propose that the psychopathological dimensions identified and validated by our study constitute a reasonable, and unique, framework for better understanding and subdividing DD.

The factor analysis used rendered an adequate model as demonstrated by a significant Barlett's test, used an adequate sample as indicated by a KMO value of 0.62, and the variation accounted for by the four psychopathological dimensions model amounts a reasonable 59.4%, while all items (symptoms) included saturated into just one psychopathological dimension (saturation >0.5), an indication of an accurate identification of latent symptomatological structures [78]. The current study cannot be compared directly to other previous studies based on factor analyses in DD because those authors focused on the characteristics of delusional ideas and attempted to group such characteristics into factors [79–81]. One possible exception might be the study carried out by Serretti et al. [53]; however, Serretti's work did not include direct interviews with DD patients, but instead, was based on retrospective medical-record assessments. Such methodological differences might explain why we found that, with the exceptions of the *Paranoid* and *Affective* dimensions, the different psychopathological dimensions in both studies do not coincide.

4.1. The psychopathological dimensions of DD

The most comprehensive and coherent combination of psychopathological dimensions, explaining virtually 60% of symptom variance, yielded a four-dimension result. In order of importance, the psychopathological dimensions were named: *Paranoid, Cognitive, Schizoid*, and *Affective*, after being comprised of a congruent core of symptoms defining such syndromic presentations in psychosis. Compared with more common studies in schizophrenic patients [82–84],

paranoid and affective symptoms are more important in DD patients, as would be expected, although cognitive symptoms were more widely present than might be expected given the classical assumption that there is no deterioration.

By and large, the *Paranoid Dimension* (PD) is the most present in the sample and consists of essential paranoia symptoms, namely, an increased presence and intensity of delusional ideation and lack of insight associated with the typical symptoms of paranoid syndrome (eg, suspiciousness, excitation, and hostility) [31,43]. The symptomatic structure of PD is comparable to what Serretti et al. [53] called "delusions", with the difference that the latter was only the third most present factor after "depression" and "hallucinations", which might be explained by the retrospective nature of this study. As in most other studies on paranoia, no significant differences with respect to gender were found, but weak associations were seen in people living alone [14]. External validity of the PD dimension is warranted by its positive association with a variety of factors that are expected to be associated with paranoidism. Thus, we found PD associated with paranoid personality disorder as established using the Standardized Assessment of Personality (SAP) [61]. Indeed, weak associations of PD with paranoid personality disorder, premorbid social isolation, and precipitating psychosocial factors were to be expected in the light of previous reports [5,16,85]. Furthermore, PD was also weakly associated with more adverse experiences of abuse and household dysfunction during childhood, something supported by both classical [5,86,87] and research studies on paranoia [88]. Similarly, a robust association was found between PD and a greater presence of legal problems resulting from violent behavior, which is consistent with studies linking violence with a higher intensity of paranoid delusions and with the fact that hostility had an important loading within this dimension [89]. In addition, PD was also strongly associated with a chronic course without remission [1,85,90] and poorer response to drug treatment, both findings well described in paranoia [20,91]. The latter findings are in line with our findings of significantly poorer treatment adherence, poorer functionality, and lower perception of social support, which could be related to the lack of insight into the disease, and to a greater degree of paranoidism. By contrast, no relationship was found with immigration or premorbid sensory-perception deficits — two risk factors for paranoid psychosis documented in previous studies [14,92,93]. Finally, multiple regression analyses revealed that the clinical variables that most strongly associated with PD were legal problems resulting from violent behavior, chronic course, lower global functioning, and poorer treatment adherence. On the whole, PD has a very similar clinical profile to the classic concept of *paranoia vera* [94] (i.e., no strange delusional ideation with paranoid syndrome in the absence of other symptoms), where psychological and environmental correlates predominate.

The *Cognitive Dimension* (CD) comprises essentially cognitive symptoms (conceptual disorganization and difficulty to think abstractly) and psychomotor symptoms (motor retardation and impaired speech spontaneity and fluency), which are more frequent in organic psychoses than in purely functional psychoses [95,96]. The validity of this psychopathological dimension is supported by its significant association with both lower scores on a standard cognitive test (MMSE) and lower educational level. CD is significantly associated with the absence of a psychiatric family history, later onset, and an increased comorbid presence of somatic pathology for which there was no clinical evidence that it was the direct cause of delusions. These results are consistent with those of the study by Lo et al., [30], who compared organic and functional DD; they are further corroborated by the notion of a subtle organic pathology in some DD cases as suggested by Munro [31]. Interestingly, the CD was also significantly associated with premorbid substance abuse, which is a subtle organic factor relevant in inducing onset of DD together with advanced age (aging) and premorbid head trauma with loss of consciousness [31]. Although high scores on CD were seen with premorbid head trauma, they did not reach levels of statistical significance. Furthermore, CD was also found to significantly and independently associate with a greater presence of hallucinations, mainly non-prominent visual hallucinations, which is to be expected in more organic psychoses [97]. All in all, the above evidence suggests that subjects with higher scores on the CD might represent a subgroup of DD patients whose delusions may be derived from mild organic brain disease heralded by poorer cognitive performance. "These findings may question the validity of the DSM-IV diagnostic criterion that the psychosocial activity alteration in DD is due solely to the impact of delusional ideation or its ramifications, and suggest that this alteration may be contributed also by, yet minor, cognitive deficits" [13]. This is further supported by our findings of poorer overall functioning, a higher degree of social disability, and more hospital admissions among DD patients with higher scores on this dimension.

The *Schizoid Dimension* (SD) comprises active social withdrawal, emotional coldness, and unusual thoughts — symptoms that are part of the DSM-IV diagnostic criteria for schizoid or schizotypal personality disorder [13]. External validity of this dimension is demonstrated by its robust, significant association with both being unmarried and having a schizoid or schizotypal personality. This is consistent with earlier reports showing the presence of schizoid and schizotypal symptoms in cases of DD [45–47]. As SD was found to associate with a history of schizophrenia in first- and second-degree relatives and schizotypal personality disorder, we posit that it is this dimension that explains that some DD cases may indeed be part of a schizophrenic spectrum of disorders [98]. Thus DD cases, particularly those loaded with higher scores on the SD, might be intermediate between paranoid schizophrenia and milder forms of DD, hence supporting the notion for a continuum between schizophrenia and milder forms of psychoses [8,48]. This can be further argued as SD was found to significantly and independently

associate with (non-prominent) auditory hallucinations in our sample, a modality that is characteristic of schizophrenia, though not typical of non-psychotic affective disorders such as some severe forms of major depression.

The association between DD and depressive syndromes has been widely documented in different studies that have reported rates ranging from 43% to 54% [26–29]. We report an *Affective Dimension* (AD), which is consistent with a depressive factor of DD detected in a previous study [53] and is comprised of feelings of guilt, somatic concern, anxiety, and depression, all of which are typical of the anxious–depressive syndrome [13]. External validation of the AD is warranted by its significant association with all other affective markers in the study, namely, increasingly severe MADRS depression scores, a comorbid diagnosis of major depressive disorder, dysthymia or anxiety disorders using the MINI, and a greater number of suicide attempts and increased suicidal risk. The AD was found to have a significant association with a positive psychiatric family history of affective illness, in line with a previous report [29], and shows higher scores (albeit not statistically significant) among women who, in turn, are more likely to suffer from affective disorders [14]. The clinical congruence of the AD described here is also supported by its significant and multivariate associations with obsessive PDs that are a well-known risk factor for affective disorders [99,100] and had been previously reported in DD of the somatic type [101–103]. Incidentally, somatic delusions were associated with the AD in this study. The finding that the AD is associated with tactile hallucinations is also in line with earlier reports of such rare hallucinations in both DD [44] and psychotic depression [104]. Finally, high scorers on the AD are less likely to present self-reference delusions that are more typical of schizophrenia and are rare when psychotic symptoms emerge within the context of affective disorders [13]. We hypothesise that the foregoing may be seen as potential evidence that some DD, particularly those with higher scores on the AD, could be at the opposite end of a continuum with those with high SD scores and, possibly, closer than the latter to affective disorders.

4.2. Limitations and implications for clinical diagnosis

One limitation of our study is its relatively small sample size, given the low prevalence of DD (< 0.1%) and the low number of delusional patients seeking treatment [14]. This limitation leads to a less reliable estimation of correlations between the PANSS items that could possibly jeopardize the stability of the factor analysis. Additionally, it is particularly difficult to recruit a large enough sample with rare DD types (somatic, erotomaniac, and grandiose) to conduct multivariate analyses. Due to the relatively small size for a factor analysis, the interpretation of our results should be taken with caution as estimation of effect sizes, artificial rising of typical error estimations, external validity and overall generalization of results, maybe partially limited [105]. Despite this, the DELIREMP study, a systematized study using a large number of variables, reports on what is, to our knowledge, the largest sample of all cross-sectional studies on DD in the literature. Our study may also be limited by the selection bias resulting from the need to have the referring psychiatrist's permission to participate (the final sample may have been composed of patients with less severe DD). Yet, lacking broader empirical studies, the present report constitutes to our mind an unprecedented break-through in the empirical knowledge of actual DD symptom identification. All diagnoses and psychopathological assessments were made by a single fully-trained clinical psychiatrist whilst all neuropsychological assessments and other clinical data were collected by a single clinical psychologist. In addition, we did not include a control group with other psychoses patients to entirely explore the DD specificity of the described dimensions.

Our study identifies and validates four psychopathological dimensions for DD (paranoid, cognitive, schizoid, and affective), which, while presenting homogeneous symptom structures, take on greater clinical validity by displaying consistently congruent associations with sociodemographic and clinical phenomena. This study is, to the best of our knowledge, the first to demonstrate the true, empirically-determined, nature of DD phenomenological variation. In the light of our findings, the current DSM-IV or ICD-10 classification of DD can be questioned, as it is based on theoretical, aprioristic and not-empirical descriptions of, mainly, delusional content determining unvalidated DD subtypes of limited clinical utility [106,107]. This may partially explain much of the reputation DD has for being treatment-resistant. A more informed assessment of DD patients geared toward identifying individual expression of psychopathological dimensions, like the ones reported here, can contribute to tailoring treatment strategies that specifically target each DD patient's personal symptom profile. Nonetheless, further knowledge on this topic is urgently needed, as the prevalence of DD may be much higher than previously thought [52] and future studies should replicate and/or further validate our psychopathological dimensions, ideally by including neuropsychological, genetic, neurophysiological, or neuroimaging techniques that could also help to identify endophenotypes to better describe DD and other psychotic categories.

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