Schizophrenia Bulletin vol. 38 no. 3 pp. 561–568, 2012
doi:10.1093/schbul/sbq125
Advance Access publication on November 15, 2010

Delusional Disorders—Are They Simply Paranoid Schizophrenia?

Andreas Marneros*, Frank Pillmann, and Tobias Wustmann

Department of Psychiatry, Psychotherapy, and Psychosomatics, Martin Luther University of Halle-Wittenberg, Julius-Kühn-Strasse 7, 06097 Halle/Saale, Germany

*To whom correspondence should be addressed; tel: 49345-557-3651, fax: 49345-557-3607, e-mail: andreas.marneros@medizin.uni-halle.de

Objectives: **This article tries to give an answer to the question of whether *International Classification of Diseases* (*ICD-10*) persistent delusional disorder (PDD) or *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*) delusional disorder (DD) is simply paranoid schizophrenia (PS). Because *ICD-10* PDD and *DSM-IV* DD are identical, we use DD as a synonym. Methods: A prospective and longitudinal study compared all inpatients with DD treated at the Halle-Wittenberg university hospital during a 14-year period with a previously investigated selected cohort of patients with PS. Sociodemographic data, symptomatology, course, and outcome parameters were examined using standardized instruments. The duration of the follow-up period in patients with DD was 10.8 years and for the PS patients 12.9 years. *Results:* Significant differences between DD and PS were found: DD patients are, in comparison to patients with PS, significantly older at onset. Less of their first-degree relatives have mental disorders. They less frequently come from a broken home situation. First-rank symptoms, relevant negative symptoms, and primary hallucinations did not occur in patients with DD. Patients with DD were less frequently hospitalized, and the duration of their hospitalization was shorter. Their outcome is much better regarding employment, early retirement due to the disorder, and psychopharmacological medication. They more often had stable heterosexual partnerships and were autarkic. They had lower scores in the Disability Assessment Scale and in Positive and Negative Syndrome Scale. The diagnosis of DD is very stable over time. *Conclusions:* The findings of this study support the assumption that DDs are a separate entity and only exceptionally can be a prodrome of schizophrenia.**

Key words: persistent delusional disorders/schizophrenia/course/outcome/classification

Introduction

Delusional disorders (DDs) have a long tradition, being the successor of the paranoia concept, which, in the 19th and at the beginning of the 20th century, was fundamental in psychiatry. Due to the reform of the paranoia concept by Emil Kraepelin,[1] who defined the condition in a very narrow sense, and the creation of the schizophrenia concept by Eugen Bleuler[1,2] the diagnosis of "paranoia" was marginalized. Some authors, eg, Kurt Schneider,[3] declared: "Paranoia is dead. It is simply schizophrenia." Because of several misunderstandings, George Winokur[4] introduced the term "DD," meaning exactly the same as the last version of Kraepelin's paranoia.[1] The term DD has been "officially" introduced in the diagnostic nomenclature by *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised* (*DSM-III-R*). *International Classification of Diseases* (*ICD-10*) defined "persistent delusional disorder" (PDD) almost in the same way as *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*) DD; hence, both terms can be used synonymously. The difference in the chronological criterion (*ICD-10*: 3 mo, *DSM-IV*: 1 mo) can practically be neglected because in clinical reality, DDs persist much longer.[5] We decided to use the term DD in this article. Because DDs are not very common, they amount to approximately 0.03%–0.18% of a general population and 0.4%–4% of a hospital population[5–7]; there is a lack of investigations, especially of longitudinal biological and genetic studies, regarding the disorder as defined in *ICD-10* and *DSM-IV*. Thus, the question of their relation to schizophrenia has not yet been answered satisfactorily.[5,8] Of course, there are studies reporting on a position of DD separate from schizophrenia, like those of Winokur[4] and Kendler[6] or those of the "Scandinavian school"[9,10] and the "Vienna school"[11], but the definitions and instruments used in these otherwise important studies were usually different from the modern ones.

The aim of this article, which is part of the Halle Delusional Syndromes Study (HADES Study), is to contribute to answering the question of the relation between DD as defined in *ICD-10* and *DSM-IV* and schizophrenia, comparing longitudinally patients with DD and patients with paranoid schizophrenia (PS).

Materials and Methods

Samples

Patients With PDD. The HADES Study was initiated and designed by the first author (A.M.). In the first phase of the study, all consecutive cases of PDD treated as inpatients at the Department for Psychiatry, Psychotherapy, and Psychosomatics at the Martin Luther University Halle-Wittenberg, Germany, between 1994 and 2008, ie, during a period of 14 years ($N = 9969$), were identified. All patients were first diagnosed in the postpharmacological era. The hospital serves a large municipal and suburban catchment area with a nonselective admission policy. Patients with a clinical discharge diagnosis of PDD were considered for inclusion in the study. For inclusion in the study, all these diagnoses were reviewed independently by the authors on the basis of a checklist consisting of the *ICD-10* research criteria for PDD and the *DSM-IV* criteria for DD. Only subjects who were confirmed to fulfill both the diagnostic criteria of PDD of *ICD-10* (F22) and DD of *DSM-IV* (297.1) were included. Out of initially 61 patients with DD, 43 patients fulfilled these criteria during the above-mentioned period of 14 years.

Follow-up investigations took place at 10.8 ± 4.7 years after onset of the disorder or 6.6 ± 3.8 years after the index hospitalization. After this time, these patients were reassessed and asked to give their informed consent to take part in an assessment of various psychiatric and psychological constructs. Of the original sample, 33 patients participated in the follow-up examination. At the time of follow-up, only 7 patients refused consent, 3 had died (one of them presumably by suicide), and the remaining 33 subjects were personally interviewed, which amounts to 77% of the surviving patients.

Patients With PS. The PS control group was composed of 42 inpatients with PS according to *DSM-IV* criteria treated at the same hospital department between 1993 and 1997. This sample has originally been selected as a control group in a study on acute and transient psychotic disorders.[12] It has therefore a higher proportion of females and a slightly later onset of the disorder than unselected patients with schizophrenia. Despite this limitation, we decided to use this sample for our comparison with the DD patients because patients with PS appear to be adequate controls for a comparison with patients with DD. Possible influences of gender will be discussed in the Discussion and Conclusions section. Thus, a more favorable outcome for DD patients (as hypothesized) could not be attributed to the composition of the control group and would even be more valid. The PS sample and the details of recruitment and data acquisition have been described previously.[13,14] The patients have been investigated in 3 waves of follow-up investigations at predetermined times 2.5, 5, and 7 years after the index episode or at a mean of 8.6 ± 7.8, 10.5 ± 7.3, and 12.4 ± 7.3 years after the first episode. Data from at least one point of follow-up could be obtained from 91.7% of the original sample. For the present comparison, for each subject, data were used from the last follow-up investigation available resulting in mean follow-up times of 12.9 ± 7.8 years after the onset of the disorder.

Instruments

During the study, a variety of instruments were used.[5] Those used for the findings referred to in the present article are described below. We systematically recorded demographic, social, and clinical features. Information was gathered using a semistructured interview already used in earlier studies,[15] hospital records, and, where available, information from family members or other suitable sources. *DSM-IV* diagnoses for the index hospitalization and lifetime diagnoses were assessed with the Structured Clinical Interview for *DSM-IV*[16]; *ICD-10* diagnoses were assessed according to the *ICD-10* research criteria.[17] The classification of socioeconomic status followed the criteria of Kleining and Moore,[18] who in turn largely adapted the classification of Hollingshead and Redlich.[19] Educational level was considered very low for subjects with less than 8 years of schooling or special education, low for subjects with 8 or 9 years of schooling, medium for subjects with 10 or 11 years of education, and high for subjects with 12 or more years of education. For the evaluation of psychopathological parameters reviewing the index hospitalization, a symptom list derived from the Brief Psychiatric Rating Scale[20] and the Manual of the Association for Methodology and Documentation in Psychiatry[21] was used. Items were rated as ''present'' or ''absent.''

Relapse was defined as the occurrence of a major affective syndrome or of psychotic symptoms leading either to hospitalization or to outpatient treatment, including psychiatric medication and a disruption of daily activities. A limitation of this definition, however, was given by the fact that in most of the DD patients, the delusional symptoms persisted more or less during the whole follow-up period. For such patients, hospitalizations during follow-up not necessarily meant a dramatic exacerbation of symptoms or deterioration, but most frequently the rehospitalization was a result of social conditions.

Psychopathological symptoms at follow-up were assessed with the Positive and Negative Syndrome Scale (PANSS).[22]

The level of general functioning was assessed using the Global Assessment of Functioning Scale (GAF). The GAF is a widely used rating scale for the evaluation of the overall functioning of a subject during a specified period on a continuum that ranges from a state of severe psychiatric illness to a state of health. The Social and Occupational Functioning Assessment Scale (SOFAS) was used to assess the individual's level of social and occupational functioning not directly influenced by the overall severity of psychiatric symptoms. The reliability and validity of GAF and SOFAS are well documented.[23] Social disability was measured using the German version of the WHO Disability Assessment Schedule (DAS).

All interviewers are physicians and were extensively trained in the use of the instruments by a senior consultant (F.P.). Interrater reliability for the instruments in our group has been determined and found to be good to excellent.[24]

Statistical Analyses

Statistical analyses were performed with the Statistical Package for Social Sciences version 17.0. Bivariate comparisons of continuous data were performed with 2-tailed *t* tests. χ^2 tests of Fisher's exact test were used for contingency tables of categorical data where appropriate. For the comparison of quantitative data, *t* tests or Mann-Whitney *U* tests were used as appropriate. ANOVAs were calculated with Scheffé post hoc tests if indicated. Significance was assumed with $P < .05$.

Ethical Issues

Patients were approached and asked for participation in a state when they were able to understand the procedure. All subjects provided written informed consent. The study protocol was approved by the local ethics committee.

Results

The results of the comparison of various variables of DD and PS are displayed in tables 1–5. The following differences were found to be statistically significant.

Age at Onset

Patients with DD became ill significantly later than patients with PS (46.6 vs 35.3 y). Thus, DD patients experienced the onset of their disorder more than 10 years later than those with PS (table 1).

A broken home situation was found to be more frequent in patients with DD than in patients with PS. "Broken home situation" was defined as a disruption in the continuity of caregiving in the patient's family before the age of 15 (when one of the following criteria was met: death of one or both parents, divorce or separation of parents, care persons other than parents, severe addiction of one or both parents[25]) (table 1).

A detailed "family history" was obtained for all subjects. Data did not allow a differentiation between different psychotic and major affective disorders, but an attempt was made to differentiate nonorganic psychotic and nonorganic affective disorders from other mental disorders (eg, alcohol dependency). A positive family history was more frequent in patients with PS when compared with DD, although this difference reached only trend significance when all diagnoses were considered, but no statistical significance at all was found for nonorganic psychotic and affective disorders (table 1).

Index Hospitalization

As mentioned previously, the age at onset in DD is more than 10 years higher than that in PS. This time difference is reflected in the index episode (table 2).

The "duration of the index hospitalization" was significantly longer for patients with PS. There were no differences in involuntary admissions or discharge against medical advice. Roughly equal proportions of DD and PS patients experienced a stressful life event during the 6 months prior to the index admission. Both groups had higher rates of stressful life events preceding the onset than the index admission (table 2).

Symptomatology During Index Hospitalization

As table 2 shows, "per definitionem," all patients had delusions, but bizarre delusions, primary hallucinations, and other primary first-rank schizophrenic symptoms[3] occurred exclusively in patients with PS, which, however, is a function of definition. In DD, secondary hallucinations (such as tactile or olfactory hallucinations deriving from the delusional context) rarely occurred (18.6%). Anxiety was found to be significantly more frequent in PS (53.7%) than in DD (16.3%). Depressed mood (not fulfilling the criteria of major depression or other depressive episodes), negative symptoms such as flat affect or alogia, only occurred in PS patients and were not found in DD patients.

Course and Outcome

DDs show a remarkable diagnostic stability over time. Only 7 patients (21.2%) of the DD group shifted into schizophrenia or schizoaffective disorder (only 1 patient, manic type) during a period of 10.8 years; in 78.8% of the patients, no such syndrome shift was found. The syndrome shift in DD occurred after a mean of 7.68 (4.7) years (table 3). All patients with syndrome shift but one had delusions of the persecutory type; only one had erotomania. All patients with syndrome shift but one were men; females showed a higher diagnostic

Table 1. Relevant Sociobiographical Data

	DD $n = 43$		Paranoid Schizophrenia $n = 42$		P
Age at onset in years (mean ± SD)	46.9	13.2	35.3	13.9	<.001[a]
No. of previous episodes (mean ± SD)	0.47	1.6	1.76	2.05	<.001[a]
Birth complications (*n*, %)	4	9.3	4	9.5	>.999[b]
Developmental disturbance (*n*, %)	4	9.3	5	11.9	.738[b]
"Broken home" situation (*n*, %)	14	32.6	26	61.9	.007[c]
Mental illness in first-degree relative (any disorder) (*n*, %)	10	23.3	17	40.5	.088[c]
Mental illness in first-degree relative (only psychotic or major affective disorders) (*n*, %)	5	11.6	7	16.7	.505[c]
Mental illness in first-degree relative (affective disorders) (*n*, %)	4	9.3	0	0.0	.116[b]
Mental illness in first-degree relative (psychotic disorders) (*n*, %)	1	2.3	7	16.7	.030[b]
Educational level					
Very low (*n*, %)	3	7.0	4	9.5	.654[d]
Low (*n*, %)	18	41.9	14	33.3	
Medium (*n*, %)	12	27.9	21	50.0	
High (*n*, %)	10	23.3	3	7.1	

Note: delusional disorder, DD
[a]*t* test.
[b]Fisher's exact test.
[c]χ^2 test.
[d]Mann-Whitney *U* test.

stability.[26] Patients with syndrome shift were excluded from the following analyses of outcome measures. Outcome measures therefore refer to "pure" DD; patients with DD having additional mood episodes during course were not excluded because these proved to be independent of the DD. The DD persisted after the remission of the mood symptomatology, which was not the case when the patients had shifted to schizophrenia or schizoaffective disorder.

Patients (61.6%) with DD did not have subsequent admissions after first hospitalization, but significantly more schizophrenic patients (78.4%) had further hospitalizations, and therefore, the number of hospitalizations is significantly higher in the group of patients with PS than in the DD group (table 3).

The "psychosocial status" at follow-up for the two clinical groups is given in table 4. DD patients show a more favorable outcome in all aspects, which is statistically significant in all areas. In particular, much more patients with DD were employed, and they had significantly lower rates of early retirement due to their mental disorder (only half as many as patients with PS). Most patients with DD (88.5%) retained their autarky (ie, their capability of independent living with or without receiving support from other family members), whereas this is true only for 60.5% of the PS patients. Significantly more PS patients (89.2%) than DD patients (53.8%) received psychopharmacological medication.

The outcome parameters shown in table 5 are significantly more favorable for DD than for PS patients. Generally, mean outcome was more favorable for DD than for PS. Social disability was significantly more pronounced for PS. At follow-up, PS patients suffered from more negative symptoms in the PANSS and from more general symptoms and they also had a higher total score than DD. The difference in outcome is not reflected in the Global Functioning Score, which probably reflects the fact that delusional symptoms persisted in the majority of DD patients throughout the follow-up period.

Discussion and Conclusions

The longitudinal comparison of patients with the *DSM-IV* diagnosis DD or the *ICD-10* diagnosis PDD (which can be used as synonyms) and patients with PS, relevant differences between the two groups become evident, most of which concern course and outcome parameters, age at onset, family history for mental disorders, and symptomatological level.

Table 2. Characteristics and Symptomatology of the Index Hospitalization

	DD $n = 43$	Paranoid Schizophrenia $n = 42$	P
Age at index admission (mean, SD)	51.8 (12.6)	41.1 (12.4)	<.001[a]
Duration of index hospitalization in days (mean, SD)	38.7 (27.6)	78.7 (51.5)	<.001[a]
Involuntary admission (*n*, %)	8 (18.6)	4 (9.5)	.229[b]
Discharge against advice (*n*, %)	9 (20.9)	6 (14.3)	.422[b]
Life events before index admission (*n*, %)	9 (20.9)	9 (21.4)	.955[b]
Life events before onset (*n*, %)	19 (44.2)	16 (38.1)	.568[b]
Symptomatology			
Delusions (*n*, %)	43 (100)	41 (97.6)	.494[c]
Hallucinations (*n*, %)	8[d] (18.6)	39 (92.9)	<.001[b]
Anxiety (*n*, %)	7 (16.3)	22 (52.4)	<.001[b]
Depressed mood (*n*, %)	24 (55.8)	37 (88.1)	.001[b]
First-rank symptoms (*n*, %)	0	36 (85.7)	<.001[b]
Bizarre delusions (*n*, %)	0	30 (71.4)	<.001[b]
Flat affect (*n*, %)	0	12 (28.6)	<.001[b]
Alogia (*n*, %)	0	9 (21.4)	.001[c]
Apathy (*n*, %)	0	1 (2.4)	.494[c]

Note: delusional disorder, DD
[a]*t* test.
[b]χ^2 test.
[c]Fischer's exact test.
[d]Secondary tactile ($n = 2$) or olfactory ($n = 6$) hallucinations in the background.

Regarding "long-term outcome," significantly more patients with DD than patients with PS were not impaired in autarky (ie, living independently without social support) (88.5% vs 60.5%), were still employed (56.3% vs 15.6%), had better scores in the DAS (1.04 vs 2.18), and better total scores in PANSS (41.2 vs 56.9) as well as in its

Table 3. Hospitalizations During Follow-up in Patients With Delusional Disorder (DD) and Paranoid Schizophrenia (PS; Only Patients With Follow-up)

	DD $n = 33$	PS $n = 38$	P
Age at follow-up (mean, SD)	57.7 (11.7)	47.3 (11.6)	<.00[a]
With further hospitalizations during follow-up (*n*, %)	13 (39.4)	30 (78.9)	.001
No. of hospitalizations during follow-up period/year (mean, SD)	0.12 (0.21)	0.32 (0.35)[b]	<.001[c]
At least one hospitalization due to			
DD (*n*, %)	5 (15.2)	0	.018[d]
Schizophrenic episode (*n*, %)	6 (18.2)	26 (68.4)	<.001[b]
Affective episode (*n*, %)	9 (27.3)	2 (5.3)	.011[b]
Acute and transient psychotic disorder episode (*n*, %)	0	6 (15.8)	.027[d]
Schizoaffective episode (*n*, %)	1 (3.0)	2 (5.3)	>.999[d]
Other/unclear episode (*n*, %)	0	6 (15.8)	.027[d]
DD patients without syndrome shift (pure DD) (*n*, %)	26 (78.8)	—	—
Time of syndrome shift in "pure DD" in years after onset (mean, SD)	7.68 (4.7)	—	—
Without further hospitalizations (*n*, %)[e]	19/26 (73.1)	8 (21.6)	<.001[b]

[a]*t* test.
[b]χ^2 test.
[c]Mann-Whitney *U* test.
[d]Fisher's exact test.
[e]only pure DD.

Table 4. Outcome: Psychosocial Variables at Follow-up (Only Patients With Pure Delusional Disorder [DD] Confirmed at Follow-up)

	Pure DD n = 26 n (%)	Paranoid Schizophrenia n =38 n (%)	P
Employed (only subjects < 60 y)	9/16 (56.3)	5/32 (15.6)	.006[a]
Early retirement due to mental disorder	9 (34.6)	26 (68.4)	.008[b]
Autarky (living independently)	23 (88.5)	23 (60.5)	.015[b]
On psychopharmacological medication	14 (53.8)	34 (89.5)	.001[b]

[a]Fisher's exact test.
[b]χ^2 test.

partial scales for general and negative symptoms (21.6 vs 27.2 and 8.6 vs 18.6). In contrast, the schizophrenic patients retired significantly more frequently due to their disorder than patients with DD did (68.4% vs 34.6%). They also received more frequently psychopharmacological medication (89.2% vs 53.8%) and more frequently needed hospitalization. In other words, the social and functional prognosis of DD, in spite of the persistence of its monothematic and monosymptomatic delusions, was significantly better than that of schizophrenia. A better prognosis of DD compared with schizophrenia was also reported in other studies, like those of Opjordsmoen,[10] Opjordsmoen and Retterstol,[27] Berner et al,[28] or Stephens et al.[29] The prognostic argument is an important support for the assumption that DDs are not schizophrenia.

Another important argument in favor of the assumption of two separate entities is the high "stability of the diagnosis" of DDs over time.[4,6,29,30] In the present study, a stable diagnosis over more than 10 years was found in almost 79% of the patients with DD. Only 6 patients (18.2%) changed into schizophrenia and one (3.0%) into schizoaffective disorder. The diagnostic stability of DD is significantly higher than that of acute and transient psychotic disorder, of bipolar schizoaffective disorder,[12] or of unipolar schizoaffective disorder,[25] and it is equivalent to the high diagnostic stability of schizophrenia.[30,31]

Another relevant finding supporting the assumption of the independence of DD was the difference in "age at onset": Patients with DD became ill for the first time at a higher age than schizophrenic patients, a finding which is compatible with previous studies, for instance, by Winokur[4] and Kendler,[6] whose conclusions were based on the analysis of many other previous studies. The finding is also compatible with more recent studies, for instance, those of Yamada et al[32] or Grover et al.[33]

Whether there are also differences between DD and PS regarding "gender distribution," is not yet clear. The HADES Study did not find any significant differences in gender distribution in the DD patients (51.2% males vs 48.8% females).[26] In the present article, a comparison of the DD and PS groups regarding gender distribution is not possible because the group of schizophrenic patients

Table 5. Outcome: Social Disability, Psychological Impairment and General Functioning at Follow-up (Only Patients With Pure Delusional Disorder [DD] Confirmed at Follow-up)

	Pure DD n = 26	Paranoid Schizophrenia n = 38[a]	P[b]
Disability Assessment Schedule Global Score[c] (mean, SD)	1.04 (0.99)	2.18 (1.63)	.002
Positive and Negative Syndrome Scale			
Positive symptoms[c] (mean, SD)	11.0 (3.2)	11.2 (6.3)	.897
Negative symptoms[c] (mean, SD)	8.6 (3.1)	18.6 (8.9)	<.001
General symptoms[c] (mean, SD)	21.6 (4.5)	27.2 (9.1)	.006
Total score[c] (mean, SD)	41.2 (8.5)	56.9 (21.3)	.001
Global Assessment Score[d] (mean, SD)	62.7 (16.5)	60.0 (22.4)	.608
Global Assessment of Functioning Scale > 70 (n, %)	8 (30.8)	15 (39.5)	.476[e]

[a]For Positive and Negative Syndrome Scale (PANSS), n = 27 due to missing data.
[b]t test if not otherwise indicated.
[c]Possible scores range from 0 to 5, higher scores indicate higher deficit.
[d]Possible scores range from 0 to 100, higher scores indicate better functioning.
[e]χ^2 test.

was adjusted regarding gender distribution to a control group with acute and transient psychotic disorder[12]. The balanced proportion between genders in schizophrenia, however, can be assumed to be a very stable finding. Regarding DD, some authors found a clear overrepresentation of men,[4] others found a moderate overrepresentation of men,[6] other studies, for instance, the present one or that of Hsiao et al,[34] found an approximate balance between the two genders, and yet others found an overrepresentation of women.[32,33,35] Hence, the findings of these studies do not allow a conclusion on whether there is in fact a gender difference between DD and PS.

Regarding the "symptomatological level," it can be said that the presence of delusions is the only similarity between DD and PS. All other symptoms, eg, hallucinations, anxiety, or depressed mood, either occurred significantly more frequently in PS or they did not at all occur in DD, for instance, first-rank schizophrenic symptoms, flat affect, alogia, or apathy.

Patients with PS more frequently had first-degree relatives with mental disorders than patients with DD (40.5% vs 23.3%).

Summarizing the findings of the present study, the following can be concluded:

1. The only relevant symptomatological similarity between DD and PS is the fact that the core characteristic of DD, namely, delusions, can also be a symptom in schizophrenia.
2. PS is polysymptomatic, also in regard to a variety of psychotic symptoms, whereas DD is monosymptomatic regarding the psychotic symptomatology.
3. PS usually includes so-called negative symptoms, but DD does not, at least not to a relevant extent.
4. In PS, there is gender equivalence or even a majority of males, whereas in DD, there are no clear and consistent findings.
5. Age at onset in PS is lower than in DD.
6. Psychotic disorders in first-degree relatives seem to be more frequent in patients with PS than in patients with DD.
7. Only a small minority of patients with DD shift into PS after some years.
8. Social and functional outcome in DD is significantly more favorable than in PS.

Hence, it can be concluded that the differences between DD and PS are significant on many different levels, supporting the assumption that both disorders are distinct entities. The above-mentioned differences, especially regarding symptomatology and correlations, course, outcome, and family history, correspond to the criteria of Robins and Guze,[36] who can be assumed to be "validators defining a mental illness, especially schizophrenia" and in this sense separating schizophrenia from DDs. A more definite argument might be delivered by genetic-biological work. Unfortunately, there are not many studies in this area. The rare work on this topic, however, supports the assumption that DD is not a genetic variant of PS.[37–39] Cardno and McGuffin,[8] overviewing the genetic research on DD, concluded that it is not clear whether there is a genetic contribution to the etiology of DDs. Summarizing the research of family studies and family history studies on DDs, the authors concluded that DD is unlikely to be strongly related genetically to affective disorders or schizophrenia. They pointed out that the rarity of multiply affected families prohibits linkage studies, and to date, molecular genetic investigations have been mainly limited to small association studies of dopamine receptor polymorphisms. A range of considerably larger, epidemiologically rigorous studies is required, but the uncommonness and other features of the disorder strongly limit the prospects for ascertaining adequate samples.[8]

Nevertheless, the data of clinical and prognostic studies support the assumption that DDs are not simply schizophrenia but obviously an independent entity. Hence, the results of the above study confirm the opinion of the creators of the concept of DDs, for instance, Kraepelin[1] or Winokur,[4] agreeing with Eugen Bleuler[40] who requested "a separate status for that not very rare disorder."

Acknowledgments

The Authors have declared that there are no conflicts of interest in relation to the subject of this study.

References

1. Kraepelin E. *Psychiatrie. Ein Lehrbuch für Studierende und Ärzte.* 8th ed. Leipzig, Germany: Johann Ambrosius Barth; 1915.
2. Bleuler E. *Dementia praecox oder die Gruppe der Schizophrenien.* Leipzig, Germany: F. Deuticke; 1911.
3. Schneider K. *Clinical Psychopathology.* New York, NY: Grune & Stratton; 1959.
4. Winokur G. Delusional disorder (paranoia). *Compr Psychiatry*. 1977;18:511–521.
5. Marneros A. *Persistent Delusional Disorders. Myths and Realities.* Cambridge, UK: Cambridge University Press; 2011.
6. Kendler KS. Demography of paranoid psychoses (delusional disorder). A review and comparison with schizophrenia and affective illness. *Arch Gen Psychiatry*. 1982;39: 890–902.
7. Perälä J, Suvisaari J, Saarni SI, et al. Lifetime prevalence of psychotic and bipolar I disorders in a general population. *Arch Gen Psychiatry*. 2007;64:19–28.
8. Cardno AG, McGuffin P. Genetics and delusional disorder. *Behav Sci Law*. 2006;24:257–276.
9. Retterstol N. *Paranoid and Paranoiac Psychoses.* Springfield, MA: Thomas; 1966.

10. Opjordsmoen S. Long-term course and outcome in delusional disorder. *Acta Psychiatr Scand*. 1988;78:576–586.
11. Berner P, Gabriel E, Kieffer W, Schanda H. Paranoid psychoses—new aspects of classification and prognosis coming from the Vienna Research Group. *Psychopathology*. 1986;19:16–29.
12. Marneros A, Pillmann F. *Acute and Transient Psychoses.* Cambridge, UK: Cambridge University Press; 2004.
13. Marneros A, Pillmann F, Haring A, Balzuweit S, Blöink R. The relation of "acute and transient psychotic disorder" (ICD-10 F23) to bipolar schizoaffective disorder. *J Psychiatr Res*. 2002;36:165–171.
14. Pillmann F, Haring A, Balzuweit S, Blöink R, Marneros A. The concordance of ICD-10 acute and transient psychosis and DSM-IV brief psychotic disorder. *Psychol Med*. 2002; 32:525–533.
15. Marneros A, Pillmann F, Haring A, Balzuweit S, Blöink R. Features of acute and transient psychotic disorders. *Eur Arch Psychiatry Clin Neurosci*. 2003;253:167–174.
16. Wittchen HU, Wunderlich U, Gruschwitz S, Zaudig M. *SKID I. Strukturiertes Klinisches Interview für DSM-IV. Achse 1: Psychische Störungen.* Göttingen, Germany: Hogrefe; 1997.
17. WHO. *ICD-10 Classification of Mental and Behavioural Disorders. Diagnostic Criteria for Research 1993;Geneva, Switzerland WHO.*
18. Kleining G, Moore H. Soziale Mobilität in der Bundesrepublik Deutschland—I. Klassenmobilität. *Kölner Z Soz Sozialpsychol*. 1975;27:273–292.
19. Hollingshead AB, Redlich FC. *Social Class and Mental Illness.* New York, NY: Wiley; 1958.
20. Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. *Psychol Rep*. 1962;10:799–812.
21. Bobon D, Woggon B. The AMDP-system in clinical psychopharmacology. *Br J Psychiatry*. 1986;148:467–468.
22. Kay SR, Opler LA, Lindenmayer JP. The Positive and Negative Syndrome Scale (PANSS): rationale and standardisation. *Br J Psychiatry*. 1989;S7:59–67.
23. Hilsenroth MJ, Ackerman SJ, Blagys MD, et al. Reliability and validity of DSM-IV axis V. *Am J Psychiatry*. 2000;157: 1858–1863.
24. Pillmann F, Marneros A. Longitudinal follow-up in acute and transient psychotic disorders and schizophrenia. *Br J Psychiatry*. 2005;187:286–287.
25. Marneros A, Deister A, Rohde A. *Affektive, schizoaffektive und schizophrene Psychosen: Eine vergleichende Langzeitstudie (with summary in English)*. Berlin, Germany: Springer; 1991.
26. Wustmann T, Pillmann F, Marneros A. Gender-related features of persistent delusional disorder. *Eur Arch Psychiatry Clin Neurosci*. 2010; doi:10.1007/s00406-010-0130-1.
27. Opjordsmoen S, Retterstol N. Dimensions of delusional experiences and their value as predictors of long-term outcome. *Psychopathology*. 2007;40:278–281.
28. Berner P, Gabriel E, Schanda H. Nonschizophrenic paranoid syndromes. *Schizophr Bull*. 1980;6:627–632.
29. Stephens JH, Richard P, McHugh PR. Long-term follow-up of patients with a diagnosis of paranoid state and hospitalized, 1913 to 1940. *J Nerv Ment Dis*. 2000;188: 202–208.
30. Salvatore P, Baldessarini RJ, Tohen M, et al. McLean-Harvard International First-Episode Project: two-year stability of DSM-IV diagnoses in 500 first-episode psychotic disorder patients. *J Clin Psychiatry*. 2009;70:458–466.
31. Marneros A, Deister A, Rohde A. Syndrome shift in the long-term course of schizoaffective disorders. *Eur Arch Psychiatry Neurol Sci*. 1988;238:97–104.
32. Yamada N, Nakajima S, Noguchi T. Age at onset of delusional disorder is dependent on the delusional theme. *Acta Psychiatr Scand*. 1998;97:122–124.
33. Grover S, Biswas P, Avasthi A. Delusional disorder: study from North India. *Psychiatry Clin Neurosci*. 2007;61: 462–470.
34. Hsiao MC, Liu CY, Yang YY, Yeh EK. Delusional disorder: retrospective analysis of 86 Chinese outpatients. *Psychiatry Clin Neurosci*. 1999;53:673–676.
35. de Portugal E, Gonzalez N, Haro JM, Autonell J, Cervilla J. A descriptive case-register study of delusional disorder. *Eur Psychiatry*. 2008;23:125–133.
36. Robins E, Guze SB. Establishment of diagnostic validity in psychiatric illness: its application to schizophrenia. *Am J Psychiatry*. 1970;126:983–987.
37. Kendler KS, Hays P. Paranoid psychosis (delusional disorder) and schizophrenia. A family history study. *Arch Gen Psychiatry*. 1981;38:547–551.
38. Kendler KS, McGuire M, Gruenberg AM, Spellman M, O'Hare A, Walsh D. The Roscommon Family Study II: the risk of nonschizophrenic nonaffective psychoses in relatives. *Arch Gen Psychiatry*. 1993;50:645–652.
39. Munro A. *Delusional Disorder. Paranoia and Related Illnesses.* Cambridge, UK: Cambridge University Press; 1999.
40. Bleuler E. *Affektivität, Suggestibilität, Paranoia.* Halle/Saale, Germany: Marhold; 1906.