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Research report

Schizoaffective disorder diagnosed according to different diagnostic criteria – systematic literature search and meta-analysis of key clinical characteristics and heterogeneity

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ABSTRACT

Background: Schizoaffective disorder is viewed as a heterogeneous diagnosis among psychotic illnesses. Different diagnostic systems differ in their definition with DSM (-IIIR, -IV, and -V) providing a narrower definition than RDC and ICD-10. It is unclear whether this difference is reflected in patient samples diagnosed according to different diagnostic systems.

Methods: Exploratory study based on a systematic review of studies of schizoaffective disorder samples diagnosed by either RDC and ICD-10 (group of "broad criteria") or DSM-IIIR and -IV ("narrow criteria"); comparison (by Mann–Whitney-*U*-tests) of key characteristics, such as age, number of hospitalizations, or scores in psychometric tests, between more broadly and more narrowly defined schizoaffective disorder samples using standard deviations as a measurement of heterogeneity as well as weighted means and percentages. To reduce selection bias only studies including schizoaffective patient samples together with affective disorder and schizophrenia samples were selected.

Results: 55 studies were included, 14 employing RDC, 4 ICD-10, 20 DSM-IIIR, and 17 DSM-IV. Thirteen characteristics were compared: patients diagnosed according to broader criteria had fewer previous hospitalizations (2.2 vs. 5.4) and were both less often male (42 vs. 51%) and married (21 vs. 40%). Heterogeneity was similar in both groups but slightly higher in RDC and ICD-10 samples than in DSM-IIIR and -IV-samples: +4% regarding demographic and clinical course data and +13% regarding psychometric tests (pooled SD).

Limitations: Secular trends and different designs may have confounded the results and limit generalizability. Some comparisons were underpowered.

Conclusions: Differences in diagnostic criteria are reflected in key characteristics of samples. The association of larger heterogeneity with wider diagnostic criteria supports employing standard deviations as a measurement of heterogeneity.

1. Introduction

Regardless of the discussion about the justification of the nosological concept of schizoaffective disorder, this diagnosis is prevalent in clinical practice. According to a study in a large Medicaid sample the condition was diagnosed almost half as often as schizophrenia (Olfson et al., 2009). This finding coincides with epidemiological data: a study from Finland estimated the lifetime prevalence to be 0.32% for schizoaffective disorder and 0.87% for schizophrenia (Perala et al., 2007). Judged by the frequency of its occurrence, schizoaffective disorder is an important topic in psychiatry.

However, the diagnosis is of limited reliability. Summarizing six studies, Jäger et al. reported Cohen's kappa of schizoaffective disorder to be between 0.08 and 0.63. That is, reliability ranged from poor to bordering between moderate to substantial (Jager et al., 2011). In addition, with a kappa value of 0.37 Cheniaux and co-authors found only fair congruence between DSM-IV and ICD-10 based diagnoses of schizoaffective disorders – a considerably lower figure than those found for schizophrenia and for both bipolar as well as unipolar affective disorders (Cheniaux et al., 2009).

While the core of the diagnosis is the occurrence of both schizophrenia- and affective disorders-like symptoms, current diagnostic systems differ slightly in their criteria: DSM (-IIIR, -IV, and -V) requires schizophrenia-like psychotic symptoms in the

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absence of prominent mood symptoms (APA, 1987, 2000, 2013). Such a period is not conditional to the diagnosis of schizoaffective disorder according to ICD-10 (WHO, 1994) and to the Research Diagnostic Criteria, RDC (Spitzer et al., 1981). In the definition of RDC, schizophrenia-like symptoms in the absence of prominent mood symptoms are optional for the diagnosis. As a result, the DSM criteria can be applied to fewer patients: in a study of patients in a lithium clinic we found that fewer patients were diagnosed as schizoaffective when DSM-IIIR criteria were applied, relative to the application of ICD-10 criteria (Baethge et al., 2004), a finding supporting earlier results (Hiller et al., 1994). In this sense, we consider DSM "narrower" than ICD-10 or Research Diagnostic Criteria (RDC) (Table 1).

It is not clear whether differences in diagnostic criteria translate into differences in key characteristics of schizoaffective disorder patient samples. To the knowledge of the authors, no systematic review is available comparing samples of patients diagnosed by narrower as opposed to broader criteria, such as DSM vs. ICD.

Usually, patient samples are compared using measures of central tendency (means or medians of age, for example) or percentages (i.e., gender). In the study of schizoaffective disorders, however, it may be of particular interest to add to the comparison measures of dispersion, such as standard deviation: It is conceivable that narrower criteria may lead to narrower distributions of key characteristics in samples of schizoaffective disorder patients (e.g., age or psychometric data). In other words, samples of patients with schizoaffective disorder diagnosed according to DSM may be less heterogeneous than those diagnosed according to ICD. In a recent study, we presented such an approach to compare the heterogeneity of schizoaffective disorder, schizophrenia, and bipolar disorder (Pagel et al., 2013b).

Heterogeneity is a matter of considerable concern in psychiatry: with increasing heterogeneity regarding symptomatology, clinical course and therapeutic response of a disorder it becomes more difficult to apply general rules to its diagnosis and therapy. Also, in treatment studies on heterogeneous disorders efficacy signals may be more difficult to detect.

Accordingly, we carried out a systematic literature review and meta-analysis of studies diagnosing patients with schizoaffective disorder according to broad (ICD-10, RDC) as opposed to studies employing narrow (DSM) diagnostic criteria. Studies were compared with regard to key illness characteristics (demographical and clinical parameters) analyzing measures of both central tendency and dispersion. In order to prevent selection bias – a problem of particular importance in schizoaffective disorder research (Baethge, 2003; Pagel et al., 2013a, 2013b) – only studies were selected that included patients with schizoaffective disorder, schizophrenia, and affective disorders.

Table 1
Summary of salient diagnostic criteria for schizoaffective disorder in three different diagnostic systems

Criteria	RDC	ICD-10	DSM-IIIR and -IV
Schizophrenic and affective symptom overlap criterion	"Affective symptoms overlap temporally to some degree with an active period of schizophrenia-like symptoms"	[Affective and schizophrenic criteria] "...must be met within the same episode of the disorder [...] and concurrently for at least part of the episode. Symptoms from both [...] must be prominent in the clinical picture"	"A *disturbance (IIIR)/An uninterrupted period of illness (IV)* during which, at some time, there is either a Major Depressive or a Manic Syndrome concurrent with symptoms that meet the A criterion of Schizophrenia"
Specific time criteria	"...at least one of the [...] symptoms suggestive to schizophrenia is present during the active phase of the illness" "Signs of illness have lasted at least one week from the onset of a noticeable change in the patient's usual condition [...]"	[Schizophrenic symptoms]"...must be clearly present for most of the time during a period of at least 2 weeks" [Time criteria for affective disorder are met]	"During *an episode of the disturbance (IIIR)/the same period of illness (IV)*, there have been delusions or hallucinations for at least two weeks, but no prominent mood symptoms" "*The duration of all episodes of a mood syndrome has not been brief relative to the total duration of the psychotic disturbance (IIIR)/Symptoms that meet criteria for a mood episode are present for a substantial proportion of the total duration of the active and residual period of the illness (IV)*"
Schizophrenic symptoms	One of the following[a]: (1) Delusions of being controlled or ego-disturbances (e.g., thought broadcasting), (2) non-affective hallucinations, (3) commenting or communicating auditory hallucinations, (4) more than one week of delusions or hallucinations without prominent mood symptom, (5) more than one week of formal thought disorder without prominent mood symptoms	[One symptom out of six groups of schizophrenia like symptoms, that are very similar to the groups of symptoms provided for the defintion of schizophrenia]	Criterion A for schizophrenia
Affective symptoms	One or more distinct periods with a predominantly elevated, expansive or irritable mood (manic type) [or] dysphoric mood or pervasive loss of interest or pleasure (depressed type) [...] Specifiers for a manic syndrome or depressive syndrome	[Full criteria for one of the affective disorders]	Major depressive or manic syndrome (IIIR) or episode (IV)
Subtypes	Manic and depressive types; acute, subacute, subchronic, chronic, mainly schizophrenic, mainly affective	Manic, depressive, and mixed types, unspecified	Bipolar and depressive types
Schizophrenic and affective symptom overlap criterion	"Affective symptoms overlap temporally to some degree with an active period of schizophrenia-like symptoms"	[Affective and schizophrenic criteria] "...must be met within the same episode of the disorder [...] and concurrently for at least part of the episode. Symptoms from both [...] must be prominent in the clinical picture"	"A *disturbance (IIIR)/An uninterrupted period of illness (IV)* during which, at some time, there is either a Major Depressive or a Manic Syndrome concurrent with symptoms that meet the A criterion of Schizophrenia"

[a] This cell presents the criteria for schizoaffective disorder, manic type, according to RDC. For the diagnosis of schizoaffective disorder, depressed type, RDC demands at least one of the first three symptoms necessary for schizoaffective disorder, manic type, or one of the following: (4) more than one month of delusions or hallucinations without prominent mood symptoms, (5) preoccupation with a delusion or hallucination to the relative exclusion of other symptoms or concerns, or (6) more than one month of formal thought disorder without prominent mood symptoms.

Experience with our earlier analyses suggested that the number of samples eligible for most comparisons would be small. Also, we compared figures among different studies that varied in a host of characteristics, not only in the application of operationalized diagnostic criteria. Therefore, we consider the present analysis as explorative.

We expected that samples of patients with schizoaffective disorders diagnosed according to narrow criteria would be less heterogeneous, relative to those diagnosed by broader criteria but had no particular expectations in relation to the differences in measures of central tendency.

2. Method

This is an exploratory study based on a systematic literature search and meta-analysis. It is part of a larger study aimed at investigating the heterogeneity of samples of patients with schizoaffective disorder and at comparing schizoaffective disorder with schizophrenia and affective disorders (Pagel et al., 2013a, 2013b).

2.1. Literature search

The design have been described in detail in two earlier publications of this project (Pagel et al., 2013a, 2013b). In brief, the literature search built upon the work by Cheniaux et al. (2008) and was extended in Medline and PubMed Central (using PubMed) beyond the year 2006 until 2010. Search terms, search algorithm and inclusion as well as exclusion criteria are detailed in Table 2 and Fig. 1 (PRISMA flowchart).

As a defining element of this study, literature selection was restricted to studies that analyzed samples of patients with schizoaffective disorders along with samples of patients with schizophrenia and samples of patients with affective disorders. Titles, abstract, and – if necessary – full texts of all studies retrieved were screened by the first-author (TP). All unclear cases were discussed with the senior author (CB).

2.2. Ascertainment of data

For the present analysis, we included only studies that diagnosed patients according to DSM-IIIR or DSM-IV ("narrow criteria") or according to Research Diagnostic Criteria (RDC) or ICD-10 ("broad criteria").

We included all parameters (such as age, gender, or BPRS score) reported in the papers selected as long as they were documented in at least one publication in either group of narrow as well as broad criteria studies. Parameters included were divided into three groups: demographic parameters, clinical course parameters, and results of psychopathological or psychological scales.

2.3. Statistical analysis

The group of narrow criteria samples was compared with the group of broad criteria samples with respect to measures of central tendency (means) or to frequency (percentages) and to measures of dispersion (standard deviations). The number of studies

Table 2
Search terms, search algorithm and inclusion as well as exclusion criteria for updating the literature search (2006–2010).

Search:	(Schizoaffective OR schizo-affective) **AND** (schizophr* OR bipolar OR BD OR mani* OR cyclothymi* OR hypomania OR depress* OR affective) Limits: Clinical trial, meta-analysis, controlled clinical trial, randomized controlled trial, case reports, classical article, clinical trial Phases I, II, III, or IV, comparative study, evaluation study, historical article, journal article, multicenter study, twin study, validation study
Inclusion:	**Only studies with 3 patient cohorts**, including: Schizoaffective disorder AND Schizophrenia AND (affective, bipolar, manic, cyclothymic, hypomanic, or depressive disorder) AND **Patients diagnosed by:** ICD-10 OR DSM-IIIR OR DSM-IV OR DSM-IVTR OR RDC AND **Including studies with at least 1 parameter existing twice for:** (ICD-10 OR RDC) AND (DSM-IIIR OR DSM-IV OR DSM-IVTR) AND **At least 10 patients included**
Exclusion:	**Matched parameters** **Studies with multiple, or uncertain diagnostic criteria**

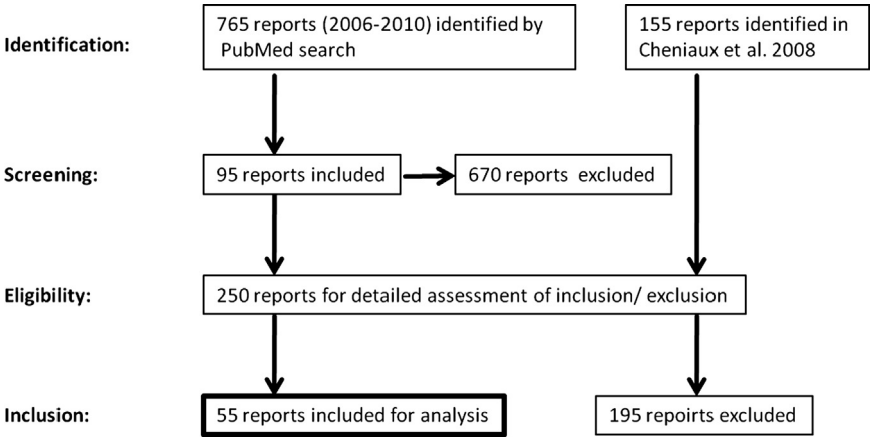

Fig. 1. PRISMA flow chart.

presenting results was small for most outcomes. Therefore, we focused on descriptive statistics. *P*-values from Mann–Whitney-*U*- or Chi-square-tests serve as an estimate of the role chance may have played in the comparisons rather than as markers of statistical significance.

Means and percentages were pooled according to the weight of the studies. Standard deviations of diagnostic subgroups were pooled using this formula:

$$\sqrt{\frac{\sum_{k=1}^{K}(nk-1)\times SDk^2}{\sum_{k=1}^{K}(nk-1))}}$$

Standard deviations of each parameter in either group (narrow vs. wide criteria studies) were standardized as percent values. The figures of the narrow group were set to 100%, and pooled standardized SDs were graphically compared by subgroup of parameters (e.g., demographic and clinical variables) as well as globally. As a safeguard, we calculated coefficients of variation (in addition to pooled standard deviations) using all pooled means and standard deviations. Also, we calculated the ratio of the sums of all 11 coefficent of variations (CV of variables of samples diagnosed according to broad criteria/CV of variables of samples diagnosed according to narrow criteria). Calculations were carried out with Excel and SPSS 21.

3. Results

Out of 920 papers initially retrieved and out of 250 papers screened, 55 studies could be included in this analysis. Of those, 14 studies employed RDC, 4 ICD-10, 20 DSM-IIIR, and 17 DSM-IV criteria. In total, the studies included 2255 patients with schizoaffective disorder (1269 in narrow and 986 in broad criteria studies) (Table 3). All studies were observational.

In total, the studies selected provided data with regard to 13 parameters. Seven parameters are demographic and clinical variables: continuous: age, age at onset, duration of illness, years of education, and number of previous hospitalizations; and nominal: gender and marital status. Six parameters relate to psychometric tests: BPRS, HAMD, IQ-test, GAS, CGI, and SANS. No biological parameter was reported in at least one study using narrow as well as one study employing broad criteria.

3.1. Measures of central tendency

Patients in studies employing broader criteria had fewer previous hospitalizations (2.2. vs. 5.4, $p=0.016$) and were slightly older (39.0 vs. 37.7 years, $p=0.035$). They were less often male (42.5 vs. 51.1%, $p=0.002$, OR: 0.71, 95% CI: 0.57–0.88) and less often married (20.5 vs. 39.7%, $p=0.064$, OR: 0.45, 95% CI: 0.17–1.13) (Table 4). Other parameters that did not reach low *p*-values but differed by more than 10% were age at onset (27.2 vs. 23.3 years), duration of illness (8.6 vs. 13.9 years), IQ (103.0 vs. 89.7). In addition, at testing, patients diagnosed by broader criteria were more depressed (HAMD: 23.6 vs. 17.0) and more burdened by negative symptoms (SANS: 56.9 vs. 41.2).

3.2. Measures of dispersion

In total, samples of schizoaffective patients diagnosed according to broader criteria were more heterogeneous than samples diagnosed by narrower DSM-criteria: When summarized for all psychometric scales, pooled standard deviation was about 13% higher. The figure for clinical and demographic variables was smaller: 4%. As a result, the global SD of "broader" groups was approximately 6% higher than that of "narrower" groups (Fig. 2).

Table 3
Studies included.

Year	Country	Study sites	Diagnosis	Number of Subjects	
				All	SA
Rieder et al. (1983)	USA	Multiple	RDC	62	15
Coryell and Zimmerman (1986)	USA	Single	RDC	97	47
Holzman et al. (1986)	USA	Multiple	RDC	85	22
Hubain et al. (1986)	Belgium	Single	RDC	53	10
Ragin and Oltmanns (1987)	USA	Single	RDC	36	12
Kiriike et al. (1988)	Japan	Single	RDC	46	10
Bellack et al. (1989)	USA	Single	DSM-IIIR	103	16
Maj (1989)	Italy	Single	RDC	88	38
Silverstein et al. (1990)	USA	Single	RDC	48	13
Kitamura and Suga (1991)	Japan	Multiple	RDC	105	24
Levinson (1991)	USA	Single	RDC	77	17
McElroy et al. (1991)	USA	Single	DSM-IIIR	78	25
Maier et al. (1993)	Germany	Single	RDC	341	115
Amador et al. (1994)	USA	Multiple	DSM-IIIR	310	49
Banov et al. (1994)	USA	Single	DSM-IIIR	173	81
Jones et al. (1994)	GB	Multiple	RDC	216	241
Sharma et al. (1994)	USA	Single	RDC	51	13
Kendler et al. (1995)	Ireland	Single	DSM-IIIR	247	40
Lewine et al. (1995)	USA	Multiple	DSM-IV	148	20
Fennig et al. (1996)	USA	Multiple	DSM-IIIR	110	17
Mitrushina et al. (1996)	USA	Multiple	DSM-IIIR	56	18
Verdoux et al. (1996)	France	Multiple	DSM-IIIR	92	14
Atre-Vaidya and Taylor (1997)	USA	Single	DSM-IV	66	13
Manschreck et al. (1997)	USA	Multiple	DSM-IIIR	57	19
Ricca et al. (1997)	Italy	Single	DSM-IIIR	72	15
Inui et al. (1998)	Japan	Single	DSM-IV	107	12
Peralta and Cuesta (1998)	Spain	Single	DSM-IIIR	79	21
Evans et al. (1999)	USA	Single	DSM-IIIR	210	29
Gunduz et al. (1999)	USA	Single	DSM-IIIR	115	26
Mokrani et al. (2000)	France	Single	DSM-IV	134	16
Benabarre et al. (2001)	Spain	Single	RDC	138	34
Muller et al. (2001)	Ger/Austr	Multiple	DSM-IIIR	119	63
Pini et al. (2001)	Italy	Single	DSM-IIIR	206	24
Regenold et al. (2002)	USA	Single	DSM-IV	414	114
Pini et al. (2004)	Italy	Single	DSM-IIIR	156	32
Ciapparelli et al. (2003)	Italy	Single	DSM-IIIR	101	30
Schott et al. (2003)	Germany	Single	ICD-10	132	38
Jager et al. (2004)	Germany	Single	ICD-10	155	30
Advokat et al. (2005)	USA	Single	DSM-IV	85	44
Jacquet et al. (2005)	France	Multiple	DSM-IIIR	320	63
Nardi et al. (2005)	Brasil	Single	DSM-IV	173	61
Glahn et al. (2006)	USA	Single	DSM-IV	56	15
Ciapparelli et al. (2007)	Italy	Single	DSM-IV	98	19
Martin et al. (2007)	USA	Single	DSM-IV	87	18
Richardson et al. (2007)	USA	Single	DSM-IIIR	240	59
Radonic et al. (2008)	Croatia	Single	DSM-IV	45	15
Szoke et al. (2008)	France	Multiple	DSM-IV	166	26
van Winkel et al. (2008)	Belgium	Single	DSM-IV	707	92
Lambert et al. (2009)	Germany	Single	ICD-10	2175	249
Ledda et al. (2009)	Italy	Single	DSM-IV	41	11
Lencz et al. (2009)	Usa	Single	DSM-IV	349	61
Ongur et al. (2009)	USA	Single	DSM-IV	233	61
Reichenberg et al. (2009)	Israel/USA	Multiple	DSM-IV	187	15
Walterfang et al. (2009)	Australia	Single	DSM-IIIR	67	15
Bottlender et al. (2010)	Germany	Single	ICD-10	177	58

At the level of single parameters eight out of eleven pooled standard deviations were larger in groups of studies diagnosed according to RDC and ICD criteria ("broader"). The raw data can be seen in Table 4. Only the comparison of the number of previous hospitalizations yielded a low probability value (3.9 vs. 1.6, $p=0.032$) (Tables 5 and 6).

When the coefficent of variance (CV) was used as a measure of dispersion results were similar: In seven out of 11 variables CV was larger in more broadly defined samples (Table 4); the unweighted ratio of CVs (CV broad/CV narrow) over all 11 variables was 1.1, indicating slightly larger dispersion in broadly defined groups.

Table 4
Means and standard deviations of schizoaffective patients defined broadly or narrow.

Category, parameter, and number of studies	RDC+ICD-10 (*n*=18)					DSM-IIIR+DSM-IV (*n*=37)				
	***N* (cases)**	***N* (patients)**	**MEAN**	**SD**	**CV**	***N* (cases)**	***N* (patients)**	**MEAN**	**SD**	**CV**
Demographical characteristics										
Age, years (*n*=48)	15	715	37.68	11.22	0.30	33	1170	38.99	10.29	0.26
Education, years (*n*=12)	3	72	11.90	3.80	0.32	9	199	12.26	3.34	0.27
Gender % (*n*=36)	***N* (cases)**	***N* (patients)**		**%**		***N* (cases)**	***N* (patients)**		**%**	
Male	9	215		42.49		27	494		51.09	
Female	9	291		57.51		27	473		48.91	
Marital status % (*n*=6)										
Currently married	1	7		20.58		5	74		39.78	
Course of illness characteristics	***N* (cases)**	***N* (patients)**	**MEAN**	**SD**	**CV**	**CV**	***N* (patients)**	**MEAN**	**SD**	**CV**
Age at onset. years (*n*=23)	6	285	27.20	8.55	0.31	17	464	23.30	7.38	0.32
Duration of illness, years (*n*=12)	2	48	8.57	5.04	0.59	10	318	13.92	4.63	0.33
Prev. hospitalizations (*n*=9)	4	175	2.15	1.64	0.76	5	166	5.39	3.94	0.73
Psychometric test results										
BPRS (*n*=10)	2	23	42.37	10.13	0.24	8	180	44.54	13.17	0.30
IQ (*n*=7)	3	76	102.96	14.73	0.14	4	89	89.73	12.78	0.14
HAMD (*n*=6)	2	37	23.60	9.57	0.41	4	77	16.95	7.93	0.47
GAS (*n*=6)	4	112	39.73	13.48	0.34	2	60	40.54	12.51	0.31
CGI (*n*=5)	1	249	5	1	0.20	2	49	5.54	0.77	0.14
SANS (*n*=2)	1	24	56.91	36.82	0.65	1	32	41.2	25.2	0.61

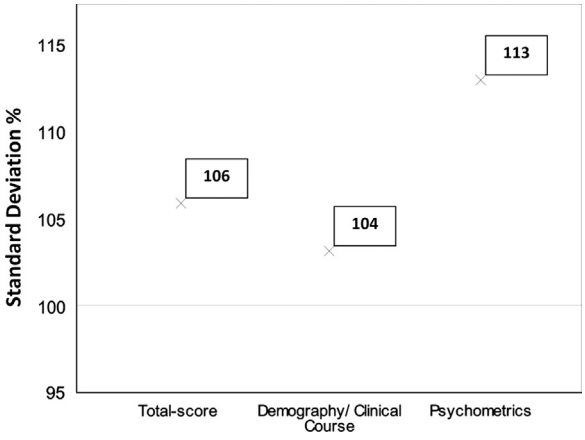

Fig. 2. Summary heterogeneity of study samples diagnosed according to broad criteria [(RDC and ICD-10), relative to narrow criteria (DSM-IIIR and -IV)]. Summary heterogeneity of studies employing narrow criteria set to 100%.

Table 5
Comparison of mean-values of single parameters.

Category, parameter, and number of studies	Rank (mean)		*P*
	RDC	DSM	
Demographics			
Age (*n*=48)	18.2	27.4	**0.035**
Education, years (*n*=12)	7.5	6.17	**0.600**
Course of illness			
Age at onset (*n*=23)	14.4	11.2	**0.319**
Duration of illness, years (*n*=12)	2.5	7.3	**0.121**
Prev. hospitalizations (*n*=9)	2.5	7.0	**0.016**
Psychometric tests			
BPRS (*n*=10)	5.0	5.6	**0.889**
IQ (*n*=7)	5.0	3.3	**0.400**
HAMD (*n*=6)	4.5	3.0	**0.533**
GAS (*n*=6)	3.0	4.5	**0.533**
CGI (*n*=5)	1.0	2.5	**0.667**
SANS (*n*=2)	2.0	1.0	**1.000**

Table 6
Comparison of standard deviations of single parameters.

Category, parameter, and number of studies	Rank (mean)		*P*
	RDC	DSM	
Demographics			
Age (*n*=48)	21.7	25.8	**0.344**
Education, years (*n*=12)	5.7	6.8	**0.727**
Course of illness			
Age at onset (*n*=23)	14	11.3	**0.431**
Duration of illness, years (*n*=12)	4.5	6.9	**0.485**
Prev. hospitalizations (*n*=9)	2.8	6.8	**0.032**
Psychometric tests			
BPRS (*n*=10)	4.5	5.8	**0.711**
IQ (*n*=7)	5.3	3.0	**0.229**
HAMD (*n*=6)	5.0	2.8	**0.267**
GAS (*n*=6)	3.5	3.5	**1.000**

Fig. 3 plots means and SD of nine variables included in the analysis.

4. Discussion

Comparing samples of patients with schizoaffective disorder diagnosed according to either RDC and ICD (broad) or DSM criteria (narrow) the present study yielded two results: Firstly, the samples differed with regard to several parameters of clinical, demographical and psychometric characteristics. Secondly, samples that were diagnosed by broader criteria were characterized by slightly more heterogeneity than samples diagnosed by narrower criteria.

It has to be borne in mind that the analyses in this study are comparisons between studies carried out at different times and in different settings. In addition to the use of different diagnostic criteria, therefore, it is likely that the studies differ in various aspects. Those differences may explain the results in part or even entirely. This seems to be particularly important for the interpretation of measures of central tendency and of frequency. For example, the percentage of married patients may depend on the area in which a

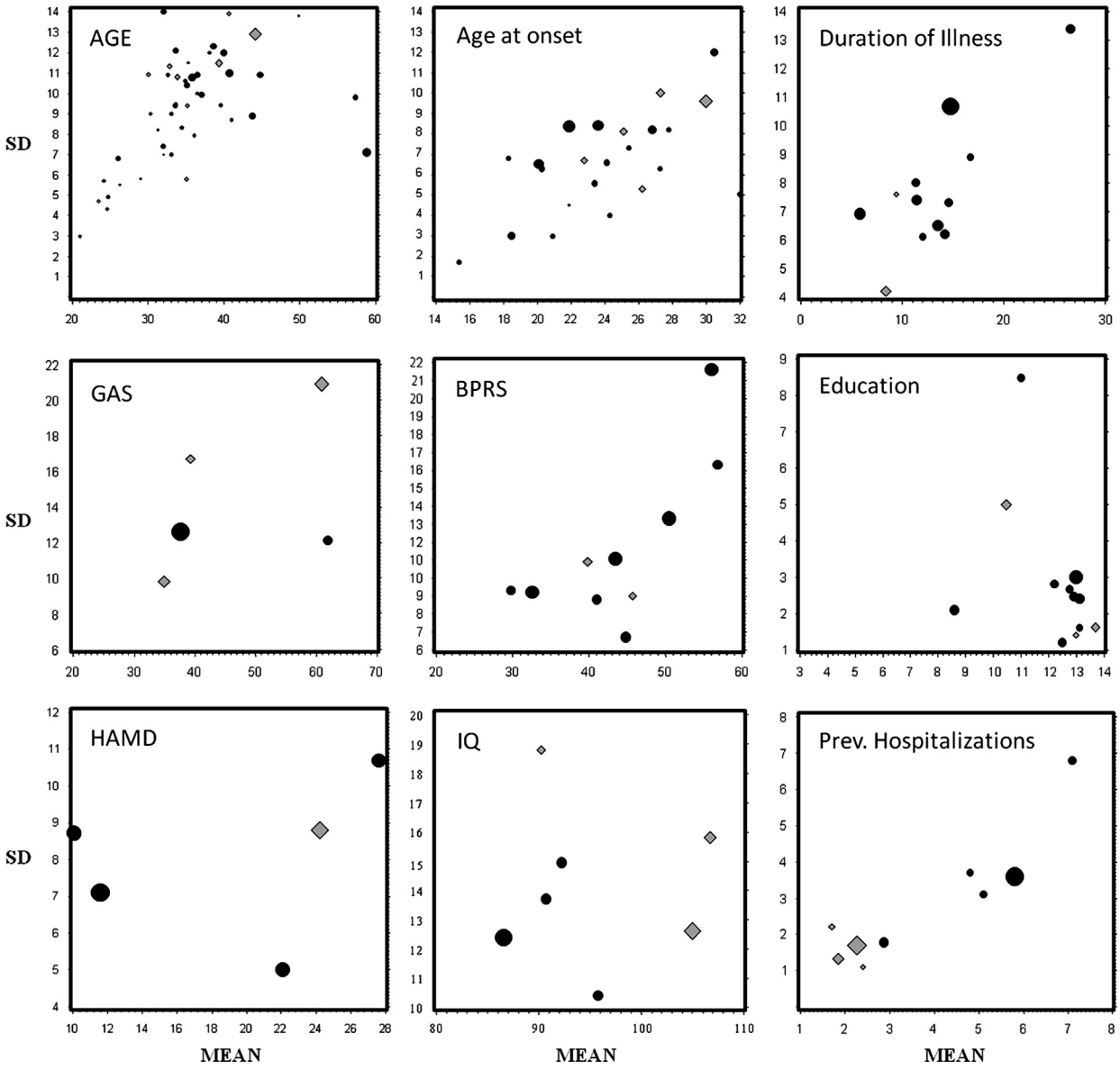

Fig. 3. Mean vs. standard-deviation for selected parameters comparing broad criteria [(RDC and ICD-10) ◇], and narrow criteria [(DSM-IIIR and -IV) ●].

study takes place (e.g., inner city vs. rural areas). It is not easy to explain by diagnostic rules why patients from samples diagnosed by DSM should have more hospitalizations or should be married more often. However, assuming that patient samples diagnosed according to DSM criteria are slightly closer to schizophrenia, and provided that, in turn, RDC and ICD criteria are closer to affective disorders, the findings of higher HAMD scores and lower BPRS scores in the latter group are plausible.

It is also possible that some study settings are more likely to draw heterogeneous samples than other settings, for example, a University Tertiary Care Center vs. a VA clinic. As a consequence, the results have to be viewed as tentative and exploratory.

However, some of the findings resonate with the use of different diagnostic criteria and may represent true differences between RDC/ICD-samples and DSM-samples. Whereas DSM-IIIR and -IV (and -V) criteria for schizoaffective disorder are closer to schizophrenia, RDC and ICD-10 criteria seem to allow the inclusion of a broader, more heterogeneous group of patients into the diagnostic entity of schizoaffective disorder. This may be reflected in larger standard deviations, our statistical measurement of heterogeneity.

On the other hand, the differences in statistical heterogeneity were small: pooled standard deviations differed by 4% for demographic and clinical data and 13% for results of psychometric tests. However, the differences among the diagnostic criteria under study are small too: The core feature of the co-occurrence of schizophrenia-like and affective disorders-like symptoms is common to all systems, and the difference results merely from DSM's requirement of a two-week period characterized by schizophrenia-like symptoms without substantial affective symptoms. Such an item is absent in ICD-10. In RDC, one of the five criteria out (only one has to be met) asks for a period of one week during which delusions and hallucinations are present without prominent mood symptoms. In this regard RDC is closer to DSM than ICD is. All in all, it is plausible that small differences in the narrowness of diagnostic criteria cause only small differences in the heterogeneity of patient samples.

The study of heterogeneity by using standard deviations is not common in psychiatry, but we have used it in an earlier study (Pagel et al., 2013b). Among the measurements of heterogeneity (e.g., range or interquartile ranges, variance, coefficient of variance) we selected standard deviation because, in our judgment, it is the measure of dispersion most often documented in psychiatric

research articles, and other measures are not inherently superior. The coefficient of variation, for example, that standardizes the standard deviation by the mean, is biased when mean and standard deviation do not increase or decrease in parallel, as in many psychometric scales. Fig. 2 illustrates that such a parallel development is apparent only in a certain number of variables. In our earlier project, however, no differences were observed when we employed both SD and coefficient of variation (Pagel et al., 2013b). In the present study too, we have used the coefficient of variation as control, and the results of this analysis supported the findings of the results based on the comparison of standard deviations. Although we believe that measuring heterogeneity may be helpful in psychiatric research, particularly in diagnostic studies, this approach and its technical specifics (such as the use of standard deviations) needs confirmation in other studies and by other researchers.

Whilst no less than 36 studies employed DSM-IIIR and -IV operationalizations, only four patient samples were diagnosed by ICD-10 criteria. This preponderance of the Diagnostic and Statistical Manual is in line with a finding by López-Muñoz et al. (2008): using a bibliometric approach, they reported that diagnostic systems, such as ICD and DSM, were increasingly mentioned in psychiatric articles between 1980 and 2005, but DSM has been used approximately five times as often as ICD.

Finally, as in every literature review, we may have missed important studies, particularly because some may not have indicated in the abstract the diagnostic system used. However, 55 studies seem sufficient to draw exploratory conclusions – the aim of the present project. On the other hand, we consider it a strength that included papers reporting on patients with schizoaffective disorder only as long as it was possible to diagnose schizophrenia or an affective disorder: Studies not allowing for these most important differential diagnoses samples of patients with schizoaffective disorder may be biased to either side – schizophrenia or affective disorders – as earlier articles have shown (Angst and Preisig, 1995; Baethge, 2003).

In summary, this study is limited by the fact that data for the parameters compared were derived from different studies. Within these limits, however, our results provide evidence that samples of patients with schizoaffective disorder diagnosed by DSM-IIIR, and -IV criteria differ in regard to clinical characteristics from those diagnosed by RDC and ICD-10. More importantly, however, they differ with regard to the heterogeneity of the sample. While this finding is no proof of the appropriateness of standard deviations as a measurement of heterogeneity, it adds plausibility to this approach. Since heterogeneity is relevant to clinical practice and to research in psychiatry, the measurement of heterogeneity may become a helpful tool for diagnostic research and for revisions of diagnostic criteria.

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Conflict of interest

None of the authors or any immediate family member has financial relationships with industrial or other commercial entities that might present the potential for conflicts of interest in the material presented.

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