Schizoaffective Disorder—Its Rise and Fall: Perspectives for *DSM-V*

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Abstract

Schizoaffective disorder, initiated in 1933, challenged the "Kraepelinian dichotomy" and Bleuler's contention that psychosis defined schizophrenia. Schizoaffective disorder recognized the diagnostic importance of mood symptoms in psychotic patients. The concept of schizoaffective disorder linked schizophrenia and bipolar disorder, stimulating comparative studies that have revealed surprising similarities and overlap between patients diagnosed with schizophrenia versus bipolar disorder. Schizoaffective disorder has increased in popularity because it appears to cover both diagnoses in psychotic patients with symptoms of mania and/or depression. The popularity of schizoaffective disorder is reflected by a PubMed search that shows over a thousand articles per year citing schizoaffective disorder for the past three years. There has been a steady increase in articles since 1975 through the present. We have reviewed a recent, selected literature addressing the validity of schizoaffective disorder as well as that comparing schizophrenia and psychotic bipolar disorders. Overlap, especially from molecular genetic and neurocognitive studies, leads to the hypothesis that schizoaffective disorder is a psychotic mood disorder and not a separate disease. Implications for the *Diagnostic and Statistical Manual of Mental Disorders-V* are discussed.

Key Words: Schizoaffective, Schizophrenia, Bipolar, Psychotic Mood Disorders, Kraepelinian Dichotomy

The Rise of Schizoaffective Disorder

Schizoaffective disorder (SAD), introduced in 1933 by Kasanin (1), is a "diagnostic compromise" between schizophrenia and psychotic mood disorder used for psychotic patients with disturbances in mood. The concept of SAD was a major diagnostic shift away from the belief that psychosis defines schizophrenia and toward recognition of greater diagnostic significance for mood symptoms. Schizoaffective disorder challenged the "Kraepelinian dichotomy" that two separate diseases cause severe mental illness by joining schizophrenia and the mood disorders; the gap between them has continued to narrow (2). "Schizoaffective psychoses," a diagnosis used by Cobb in 1943, included both schizophrenia and bipolar disorders, suggesting a single diagnostic grouping (3). SAD became established by the first *Diagnostic and Statistical Manual of Mental Disorders (DSM-I;* 1952) and its popularity is demonstrated by over 26,000 references mentioning SAD since 1949 and the substantial number of psychotic patients so diagnosed (4). The number of PubMed cites in the literature continues to increase into 2007 (see Table 1). Although SAD is no longer considered a subtype of schizophrenia, it remains more closely associated with schizophrenia than with the mood disorders in the *DSM-IV-TR* published in 2000.

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Table 1 Schizoaffective Disorder (SAD) PubMed Search

Total # Articles Citing SAD - 26,892
Total # Articles with SAD in Title - 670

Year	# Articles Citing SAD	# Articles w/SAD in Title	Year	# Articles Citing SAD	# Articles w/SAD in Title
1949	0	0	1978	542	1
1950	1	0	1979	585	14
1951	0	0	1980	516	10
1952	1	0	1981	493	11
1953	1	1	1982	579	10
1954	2	0	1983	510	18
1955	0	0	1984	589	23
1956	1	0	1985	575	13
1957	0	0	1986	558	9
1958	2	0	1987	495	11
1959	1	0	1988	548	21
1960	1	0	1989	574	22
1961	2	1	1990	583	27
1962	4	0	1991	539	19
1963	0	0	1992	555	18
1964	17	0	1993	545	17
1965	289	0	1994	585	14
1966	435	0	1995	563	17
1967	606	0	1996	613	14
1968	674	1	1997	587	19
1969	639	1	1998	623	22
1970	642	0	1999	719	27
1971	568	1	2000	731	23
1972	536	0	2001	772	31
1973	535	0	2002	757	35
1974	520	4	2003	964	27
1975	554	1	2004	907	47
1976	477	0	2005	1,084	48
1977	485	4	2006	1,108	43
			2007*	1,100	45
1949-1977	6,993	14	1978-2007	19,899	656
			1949-2007	**26,892**	**670**

*Projected

Flawed Diagnostic Criteria for SAD

The *DSM-IV-TR* Criterion A for SAD requires the presence of two syndromes: a major mood disorder, which is concurrent with two of five diagnostic symptoms that "meet Criterion A for schizophrenia" (hallucinations, delusions, disorganization of speech and behavior, catatonia and the "negative symptoms") (see Table 2). When SAD was defined, these symptoms for schizophrenia were considered disease specific. However, established bipolar patients, when psychotic, can demonstrate bizarre, mood-incongruent hallucinations (5), paranoid delusions (6), grossly disorganized thoughts and behavior (7-10), catatonia (11), the "negative symptoms" (when depressed) (12-15) and a chronic, deteriorating, treatment-resistant course (12, 13). The Criterion A symptoms for schizophrenia define "psychotic," but not any specific disorder, so Criterion A for SAD warrants rewording: instead of "symptoms that meet Criterion A for schizophrenia," substitute "psychotic." The preface of "schizo" (in schizoaffective disorder) becomes "psychotic," i.e., a psychotic affective or mood disorder.

Criterion B attempts to differentiate SAD from psychotic mood based on "at least two weeks" when hallucinations and/or delusions are present but "prominent mood symptoms" are absent. Criterion B seems flawed in two ways. First, no scientific data justifies a separate disorder based on such a two-week period. Despite the fact that several psychiatric diagnoses utilize arbitrary lengths of time in their diagnostic criteria, the very existence of SAD as separate from a psychotic mood disorder is dependent on such a two-week period. Thus, utilizing such a two-week period is particularly suspect. Furthermore, the observations of Post (12) and Goodwin (13, 14) document that well-established bipolar patients can become so psychotic that mood symptoms are obscured for weeks to months. In such cases mood symptoms are likely to be overlooked in the face of psychotic symptoms.

Symptoms diagnostic of a mood disorder have occurred (by Criterion A), and according to Criterion C for SAD, must be "present for a substantial portion of the total duration" of the illness. The second flaw of Criterion B for SAD is low reliability of eliciting such a two-week period.

No Interrater Reliability for SAD: No Validity

Cohen's kappa for the interrater reliability for diagnosing SAD is very low (0.22 and 0.19), in contrast to the kappas for mania and major depression, 0.71 and 0.82, respectively (16-19). Although some of these studies were early, the report by Maj et al. was published in 2000 (16). As recently noted by Swartz (20), " … without interrater reliability, SAD has no validity and if there is no validity, why are we using it?" In contrast to SAD, bipolar disorder is scientifically grounded with high interrater reliability and disease-specific diagnostic criteria.

We acknowledge that the mental health field in the mid-1980s was unsure about the validity of SAD and, in the absence of any diagnostic criteria in the *DSM-III*, a decision was made to introduce formal diagnostic criteria for SAD in the *DSM-III-R*, however flawed they may have been.

SAD is a Psychotic Mood Disorder

According to a recent review of 283 papers that compared schizophrenia, SAD and bipolar disorder, the major-

Table 2 ***DSM-IV-TR* Criteria (Modified for Brevity*) for Schizoaffective Disorder and Schizophrenia**

Schizoaffective Disorder (SAD)
A. Uninterrupted period of illness during which major depression, mania, or a mixed episode is concurrent with symptoms that meet Criterion A for schizophrenia†.
B. During some period of this illness there have been delusions and/or hallucinations for at least two weeks with an absence of prominent† mood symptoms.
C. Symptoms that meet criteria for mood episode are present for a substantial† portion of the total duration of active and residual periods of illness.
D. Substances and general medical conditions are excluded as causative of the above symptoms.
Schizophrenia (SZ)
A. Characteristic symptoms: two or more of the following symptoms occur during a one-month (active) phase (less if treated, except as noted below): 1) delusions‡ 2) hallucinations‡ 3) disorganized speech (frequent derailment, incoherence)‡ 4) grossly disorganized‡ or catatonic‡ behavior 5) negative symptoms (affective flattening, alogia, or avolition)‡. (NOTE: Only one symptom is required if delusions are bizarre, or hallucinations are a voice commenting on one's behavior/thoughts or two or more voices conversing with each other‡§.)
B. Social/occupational dysfunction: work, interpersonal relations or self-care have markedly deteriorated‡.
C. Duration: continuous signs for six months with one-month active phase symptoms and may include prodromal or residual symptoms‡.
D. Exclude schizoaffective and mood D/O‖ with psychotic features¶.
E. Exclude substance and general medical condition‡.
F. Exclude preexisting pervasive developmental D/O‡.

* Abbreviated format without change in meaning or substance.
† Underlines added by authors for emphasis.
‡ These criteria are disease nonspecific and occur frequently in most psychotic mood D/Os.
§ These qualifications that allow a diagnosis of schizophrenia with only one of the characteristic symptoms in section A are from K. Schneider's first rank symptoms (34), stated in 1959 but since invalidated (6).
‖ D/O = disorder(s).
¶ Mood D/Os with psychotic features are under emphasized in the U.S. and are often overlooked (7-10). As soon as psychotic symptoms are found under section A, a diagnosis of SAD or SZ is often made without adequate attention to mood symptoms (35, 38).

ity (256) suggested that SAD is on a continuum and/or is closely related to psychotic mood disorder (4). A spectrum of selected clinical and basic science studies shows overlap regarding symptom severity (7-10), course (12, 13), genetics (21-23), brain imaging (24, 25), brain metabolism and neurochemistry (26, 27), epidemiology (21), insight into their illness (28) and psychopharmacological responses (14). Such similarities should not exist if the disorders are distinct. There are no "zones of rarity" between SAD and psychotic mood disorder (29-31). A basic tenet of medicine states that when a single disease can explain the symptoms of two or more diseases, there is likely only one disease. In this case we believe that disease is usually a bipolar mood disorder because of the unique diagnostic criteria that confirm bipolar as a "bona fide" disease.

We concur that bipolar disorder is likely due to more than one genetic defect. Possibly analogous to Lesch-Nyhan disease, bipolar disorder may be caused by not only different mutations in a single gene, but also different mutations in separate genes. Regardless, we believe that the diseases now called SAD and schizophrenia are explained by psychotic mood disorders.

Conclusions

These data suggest that SAD (and schizophrenia) are mood disorders that are severe with psychotic features, not separate disorders. SAD served to initiate the concept that there were, in fact, commonalities and overlap between schizophrenia and bipolar disorder in contrast to the ideas of Kraepelin (initially), Bleuler, Schneider and many others

Table 3 Selected Quotes from Studies Comparing Schizophrenia, Schizoaffective Disorder and Psychotic Mood Disorders

Ref #	Journal/Year	Author(s)	Field of Study	Selected Quotes of Summary/Conclusions	Conclusions
4	Psychiatry Res 2006	Lake & Hurwitz	Review	"We suggest that the trend begun by Dr. Kasanin be extended to what we believe is a logical conclusion, i.e., the functional psychoses are psychotic mood disorders; there is no SAD (or SZ)."	SAD & BP same; SAD invalid
6	Arch Gen Psychiatry 1973	Carpenter et al.	Clinical Symptoms	" … these symptoms (first rank systems) which he (Schneider) considers [pathognomonic of schizophrenia] occur in 1/4 of the cohort of manic-depressive patients."	SAD & BP similar
7	Arch Gen Psychiatry 1978	Pope & Lipinski	Review (symptoms, family history & treatment response)	"The non-specificity of 'schizophrenic' symptoms brings into question all research that uses them as the primary method of diagnosis."	SZ & BP similar; SAD invalid
8	Arch Gen Psychiatry 1976	Procci	Review (symptoms, family history & treatment response)	"Schizo-Affective Psychosis: Fact or Fiction?" (article title) " … support for the adoption of some widely agreed upon epithet to describe this state (SAD) is indicated." " … at least a subgroup of these psychoses (SAD) has a definite relationship to the major affective disorders."	SAD invalid
9	Am J Psychiatry 1980	Pope et al.	Clinical Symptoms	"No significant differences were found between patients with manic disorder and SAD." "The findings suggest that SAD, as currently defined, is not a valid and independent entity."	SAD invalid
10	Psychiatr Ann 1996	Dieperink & Sands	Review (symptoms, psychotic features)	"Psychosis is prevalent in bipolar disorder … " "When differentiating from schizophrenia and schizoaffective disorder, presenting signs and symptoms are usually not helpful … "	SZ & BP similar
13	Arch Gen Psychiatry 1973	Carlson & Goodwin	Clinical Symptoms (psychotic features)	" … during acute episodes of mania, with between 50% and 80% of patients showing evidence of psychotic symptoms … at the peak of their manic episodes (patients) became grossly psychotic with disorganized thoughts, extremely labile affect, delusions, hallucinations, and brief ideas of reference."	SZ & BP similar
15	Br J Psychiatry 1970	Kendell & Gourlay	Review (symptoms, psychotic features)	" … the results of this further analysis do not lend support to the view that schizophrenic and affective psychoses are distinct entities … as most of American psychiatrists do, by glossing over the affective symptoms and regarding the illness as a form of schizophrenia … "	SZ & BP similar
20	Psychiatric Times 2002	Swartz	Editorial (clinical symptoms)	" … there is no demarcation between SAD and psychotic mood disorder." " … SAD seems an entity 'beyond necessity.'"	SAD invalid
21	Am J Med Genet 2003	Berrettini	Review (molecular genetics)	" … there are five genomic regions for which evidence suggests shared genetic susceptibility of BPD and SZ." "Family and linkage studies are consistent with the concept that SZ and BPD share some genetic susceptibility. Multiple regions of the genome, including 18p11, 13q32, 22q11, 10p14, and 8p22, represent areas with potential BPD/SZ shared genetic susceptibility."	SZ & BP similar

Ref #	Journal/Year	Author(s)	Field of Study	Selected Quotes of Summary/Conclusions	Conclusions
22	Arch Gen Psychiatry 2005	Hamshere et al.	Molecular Genetics	"Our linkage findings strongly support the existence of loci that influence susceptibility across the functional psychosis spectrum. The DISC1 gene lies within 2.5 mega bases of our peak marker on chromosome 1q42 and has been previously implicated in schizophrenia, bipolar disorder, and, recently, schizoaffective disorder."	SZ, BP & SAD similar
23	Br J Psychiatry 2005	Craddock & Owen	Editorial (molecular genetics)	"The Beginning of the End for the Kraepelinian Dichotomy." (article title) "Now molecular genetic studies are beginning to challenge and will soon, we predict, overturn the traditional dichotomous view" (that schizophrenia and bipolar are separate).	SZ & BP similar
24	Arch Gen Psychiatry 1999	Velakoulis et al.	Imaging	" … the finding of smaller left hippocampal volume in patients with first-episode schizophrenia and affective psychosis does not support the prediction that smaller hippocampi are specific to schizophrenia."	SZ & BP similar
25	Biol Psychiatry 1998	Roy et al.	Imaging	"Temporal Horn Enlargement is Present in Schizophrenia and Bipolar Disorder." (article title) " … this structural abnormality (increased temporal horn volume) does not differentiate the structural neuropathology of schizophrenia from that of bipolar disorder."	SZ & BP similar
26	Lancet 2003	Tkachev et al.	Neurochem	" … similar expression changes to the schizophrenia group in bipolar brains, which thus lends support to the notion that the disorders share common causative and pathophysiological pathways."	SZ & BP similar
27	Proc Natl Acad Sci USA 2003	Koh et al.	Neurochem	"The present study supports the hypothesis that schizophrenia and bipolar disorder may be associated with abnormalities in dopamine receptor-interacting proteins."	SZ & BP similar
28	Am J Psychiatry 2001	Pini et al.	Insight	"Patients with schizophrenia … do not differ from patients with bipolar disorder." "The lack of significant differences (in insight) between patients with schizophrenia and patients with bipolar disorder was not a result of low statistical power."	SZ & BP similar
29	Am J Psychiatry 2003	Kendell & Jablensky	Review	"Unfortunately, once a diagnostic concept such as schizophrenia … has come into general use, it tends to become reified. That is, people too easily assume that it is an entity of some kind that can be invoked to explain the patient's symptoms and whose validity need not be questioned."	NA
30	Curr Opin Psychiatry 2006	Maier et al.	Review	" … the validity of the diagnostic distinction between schizophrenia and bipolar disorder is increasingly challenged." "The diagnostic split between schizophrenia and bipolar disorder is unable to define distinct etiological and/or pathophysiological entities."	SZ & BP similar/overlap
31	Acta Psychiatr Scand 2006	Maier	Editorial	"Taken together, there is growing evidence that a substantial proportion of etiological factors is shared between schizophrenia and bipolar disorder … " "In summary, the historical starting point of the concept of schizoaffective disorders is not valid anymore … " "The task forces for new versions of the *DSM* - and *ICD*-diagnostic systems and manuals … would be badly advised if they would just continue the historical and current concepts of schizoaffective disorders into the future."	SZ & BP similar/overlap/ SAD invalid
32	Clinical Psychiatry (textbook)	Kraepelin 1913 (Taylor 1992)	Clinical Symptoms	"It is becoming increasingly clear that we cannot distinguish satisfactorily between these two illnesses (dementia praecox/schizophrenia and manic-depressive insanity/bipolar) and this brings home the suspicion that our formulation of the problem may be incorrect."	SZ & BP similar
38	Arch Gen Psychiatry 1972	Fowler et al.	Review (symptoms, psychotic features)	"The Validity of Good Prognosis Schizophrenia." (article title) " … family studies do not validate good prognosis schizophrenia as schizophrenia and suggests that most good prognosis cases are variants of affective disorder." " … the presence or absence of an affective syndrome is of considerably more diagnostic importance than schizophrenic symptoms."	SZ & BP similar
39	Acta Psychiatr Scand 2006	Vollmer-Larsen et al.	Clinical Symptoms	"A moratorium on the clinical use of the SAD diagnosis is suggested."	SAD invalid

SAD=schizoaffective disorder; SZ=schizophrenia; BP=bipolar disorder

(32-34). The "Kraepelinian dichotomy" became a cornerstone of academic psychiatry and permeated thought throughout the mental health and general medical professions. Later in his life, Kraepelin apparently reversed his "dichotomy" concept when he said, "It is becoming increasingly clear that we cannot distinguish satisfactorily between these two illnesses (dementia praecox/schizophrenia and manic-depressive insanity/bipolar) and this brings home the suspicion that our formulation of the problem may be incorrect" (35). More recently the "dichotomy" has been discounted based on molecular genetic data showing identical susceptibility loci in patients with both diagnoses (23). Despite Kraepelin's reversal, the introduction of SAD, discussion of the "continuum" theory (36, 37) and results showing substantial phenotypic and genotypic overlap between SAD, schizophrenia and bipolar disorder (21-23), the popularity of SAD seems to be increasing (see Table 1). There are some explanations for the continuing popularity of SAD (and schizophrenia) that include: 1) the absence of disease-specific pathophysiology for any psychiatric disease; 2) SAD seems to cover both schizophrenia and bipolar disorder diagnoses and so is convenient when there is diagnostic ambivalence; 3) the massive amount of research data that have accumulated on SAD and schizophrenia; and, 4) the wide acceptance of SAD and schizophrenia as a bona fide disease among the mental health and medical professions, the public at large and the media. Although we are not the first to reach this conclusion (see Table 3) (7-10, 15-17, 20, 30, 31, 38, 39), we suggest that SAD be eliminated from the *DSM-V*, and that patients diagnosed with SAD be reassessed for a psychotic mood disorder.

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