The paradigm of overlapping affective and schizophrenic spectra: schizoaffective conditions

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Broad–narrow–broad: the circuitry of certainties and uncertainties

In the centuries between the great Greek founders of medicine and psychiatry, Hippocrates, Aretaeus of Cappadocia, Galenos of Pergamon or Soranos of Ephesos (see Longrigg, 1993; Marneros and Angst, 2000; Angst and Marneros, 2001) and the father of the modern psychiatric systematics, Emil Kraepelin, at the end of the nineteenth and the beginning of the twentieth century, physicians and psychiatrists described and allocated mental disorders according to broad criteria. Symptoms, which today in modern nomenclature are called “schizophrenic,” “affective,” “mood congruent” or “mood-incongruent,” were described as characteristics of the same disorder. Therefore, case reports published during this long historic period of more than 2400 years could, with the same strong arguments, be interpreted by modern psychiatrics as “pure schizophrenia,” “pure affective disorder” or “typical schizoaffective.” At the end of the nineteenth century, Emil Kraepelin tried to clean the field, dichotomizing the so-called functional psychotic disorders into dementia praecox and manic-depressive illness (Kraepelin, 1896; 1899). The Kraepelinian dichotomy, which really was not very dichotomous, as Emil Kraepelin himself pointed out in 1920, received an epigonal strength by Kurt Schneider (1959) through the definition of “first-rank schizophrenic symptoms”: their existence confirms the diagnosis “schizophrenia” (provided that organic causal conditions can be ruled out). Kurt Schneider’s ascetic strength completed in some way Karl Jaspers’ hierarchical principle (1913). According to Jaspers’ principle, “schizophrenic” symptoms eliminate the diagnostic validity of “mood” symptoms (putting at the base of the hierarchical pyramid the “organic
symptoms” – strongest – and on the top the “neurotic” symptoms – weakest). Jaspers’ and Schneider’s influence contributes essentially to the fact that the great majority of psychiatrists of that time ignored or forgot that Emil Kraepelin himself accepted a non-classifiable domain consisting of a mixture of both conditions: schizophrenia and affective disorders. More paradoxically, it has been ignored for a long time – even by his fellows – that Kurt Schneider himself described the “cases-in-between.”

At the end of the twentieth century, it became certain that a clear dichotomy of the so-called functional mental disorders into schizophrenic and mood disorder was impossible. Clinical, prognostic, pharmacological, biological and genetic findings supported the existence of a “bridge” or a “continuum” between these disorders (Marneros et al., 1995a; 1995b).

Schizophrenic and mood disorders show overlaps. One of the efforts to identify and describe this overlapping of the spectra results in the concept of schizoaffective disorders. The major diagnostic systems, International Statistical Classification of Diseases and Related Health Problems (ICD) and Diagnostic and Statistic Manual of Mental Disorders (DSM), accept the existence of an intermediate area called “schizoaffective.” Nevertheless, the uncertainties in diagnosis and nosology remain. One of the reasons for these uncertainties is the inconsistent definition of the schizoaffective area (see below). Another reason is that the definitions of affective disorders became broader, especially in DSM-IV: mood-incongruent symptoms, even Kurt Schneider’s “first-rank symptoms,” were declared compatible with the diagnosis “mood disorder,” making the diagnosis “schizoaffective” narrower. The relativization of the diagnostic power of symptoms caused a relativization of the diagnosis as well. The boundaries between schizophrenia, schizoaffective and mood disorders became more diffuse and confused. Nevertheless, the diffusion and confusion underline more intensively the overlapping of schizophrenic and affective spectra. Its identification, however, still remains a challenge (Marneros and Tsuang, 1986; Marneros and Angst, 2000; Marneros and Goodwin, 2005a).

**Empirical efforts to identify the schizoaffective overlap**

The large group of patients who manifest the symptoms or characteristics of both major disorders – schizophrenic and mood disorder – is a challenge for theorists and clinicians. These patients present a conceptual problem to theorists, a therapeutic problem to clinicians, and a classification problem to researchers.

The problem of the “intermediate psychotic area” or the “cases-in-between” is even older than the term “schizoaffective” itself, which was originated by Kasanin (1933) (Maj, 1984; Angst, 1986; Perris, 1986; Pichot, 1986; Strömgren, 1986; Marneros and Angst, 2000; Angst and Marneros, 2001). Perhaps it began with Karl
Kahlbaum (1863) and lead through Kraepelin's work to the clinical empiricists of the twentieth century.

Karl Kahlbaum can be considered the first psychiatrist in modern times to describe some kind of “schizoaffective disorders” as a separate group in “vesania typica circularis,” applying both cross-sectional and longitudinal criteria (Kahlbaum, 1863). Nevertheless, states described as melancholia or mania by authors of the classic period, for instance by Hippocrates or Aretaeus of Cappadocia, and authors at the beginning of modern scientific psychiatry like Heinroth (1818), Griesinger (1845), or even the father of the word “psychiatry,” Johann Christian Reil (1803–12, in Marneros and Pillmann, 2005), were very often “schizoaffective” according to the modern nomenclature. Emil Kraepelin was also acquainted with cases between “dementia praecox” and “manic-depressive insanity” (Kraepelin, 1893; 1896; 1920). These “cases-in-between” (Schneider, 1959) were a problem for him, a nuisance, but on the other hand an interesting challenge. As is well known, Kraepelin dichotomized the so-called endogenous psychoses into two groups, namely “dementia praecox” (with a poor outcome) and “manic-depressive insanity” (with a favorable outcome). However, he already knew that not all cases of “endogenous” mental disorders could readily be classified into the two categories. Some cases of “mixed states,” “delirious mania,” and other mental disorders described by Kraepelin (1893; 1920) could be allocated to both categories or to neither of them. In a critical appraisal of his own taxonomy, Kraepelin wrote in his important paper of 1920 (“Die Erscheinungsformen des Irreseins” – “The Phenomenological Forms of Insanity”), that mental disorders can have elements of both groups, namely “dementia praecox” and “manic-depressive insanity” and that they can have a different course and a different prognosis than “dementia praecox” as well. He knew that the boundaries between the two groups of mental disorders are elastic and that there are bridges connecting them. His doubts became stronger in the wake of an investigation by his pupil and colleague Zendig. Zendig reported in his paper “Contributions to Differential Diagnosis of Manic-Depressive Insanity and Dementia Praecox” (1909) that approximately 30% of Kraepelin’s samples diagnosed with “dementia praecox” (using Kraepelin’s guidelines) had a course and outcome not corresponding to that of “dementia praecox”; Zendig attributed the good outcome to an incorrect diagnosis. Later Kraepelin saw in such cases a weakness of his dichotomy concept. He wrote: “The cases which are not classifiable (namely to manic-depressive insanity or dementia praecox) are unfortunately very frequent.” (Kraepelin, 1920, p. 26). Two pages later he made a decisive and for him certainly not easy statement: “We have to live with the fact that the criteria applied by us are not sufficient to differentiate reliably in all cases between schizophrenia and manic-depressive insanity. And there are also many overlaps
in this area.” (i.e., between schizophrenia and affective disorders) (Kraepelin, 1920, p. 28).

Eugen Bleuler (1911; 1924) recognized the occurrence of mood syndromes in patients he diagnosed as schizophrenic. For the most part, he ultimately concluded that schizophrenia was the illness in question and did not see these patients as a group, but rather as single, aberrant cases. Schneider (1959; 1973), in differentiating between schizophrenia and mood disorder (“cyclothymia” in his nomenclature), described “cases-in-between” in which the diagnoses of both schizophrenia or mood disorder could be made with equally strong arguments. He distinguished between concurrent and sequential forms of “cases-in-between,” and his definition bore great similarity to modern ones (Marneros et al., 1986a).

Kasanin (1933) described a group of cases which are quite “atypical” for both schizophrenia and mood disorder; so he introduced the term “schizoaffective.” These cases are fairly young individuals, socially quite well integrated, who suddenly blow up in a dramatic psychosis and present a clinical picture which may be called either schizophrenic or affective and in whom the differential diagnosis is extremely difficult. These patients had often had a history of a previous attack in late adolescence, but otherwise had good premorbid adjustment. Onset was sudden, accompanied by emotional turmoil, a distortion of the outside world and, for some, the presence of false sensory impressions, but not passivity or withdrawal. Onset was often precipitated by a definite environmental stress. The duration of symptoms would be a few weeks or months, followed by full recovery.

Kasanin’s definition was embedded in the attempt to pin down such “atypical” disorders (Marneros and Pillmann, 2005). The Norwegian psychiatrist Langfeldt (1939) added his definition of “schizophreniform psychoses,” whereby a patient’s inheritance was uncorrelated with his prognosis. He showed cyclothymic temperament, pyknic habitus, depressive symptoms, self-reference tendencies, cloudiness, incoherence, catatonic or pathoplastic features, and the illness had an acute onset characterized by distinct precipitants. Youth and good premorbid adjustment are absent from this definition.

Kant (1940) described “recovered schizophrenics” as having more bipolar affectives than schizophrenics among their relatives, pyknic physique, psychogenic precipitants of the psychotic episode, acute or sub-acute onset, duration of several months, complete recovery, clouding of consciousness, psychotic experience, ideas of reference, and auditory hallucinations. Here, family history and duration of symptoms are considered for the first time. However, Vaillant (1962) found the family history of recovered schizophrenics heavy with unipolar affectives, while the patients themselves were also typically depressed, though the operational criteria he used included acute onset, confusion or disorientation during the acute episode,
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good premorbid adjustment, a clear precipitating event, and remission to the best premorbid level.

In common, these somewhat haphazardly derived criteria for schizoaffective disorder emphasize the sudden onset, presence of confusion or disorientation, and a good recovery. The confusion or disorientation suggests a greater affinity of the illness with schizophrenia, from which it primarily differs by virtue of outcome.

Kleist (1928), continuing the tradition of Wernicke (1900) and in his tradition Leonhard (1957), described the “cycloid psychoses,” the more important features of which are the polarity of the symptoms and the favorable outcome (Perris, 1986; Marneros and Pilmann, 2005).

As early as 1966, Jules Angst investigated the schizoaffective disorders (under the term “Mischpsychosen” – “mixed psychoses”) as a part of the affective disorders. This was an outlier’s position, not only against the “zeitgeist,” but also contrary to the opinion of his teacher Manfred Bleuler, who assumed them to be a part of schizophrenia. Later investigations by Angst and his group (1989; 1990), by Clayton et al. (1968), by other members of the Winokur group (Fowler et al., 1972), by Cadoret et al. (1974) and the comparative studies of Marneros and coworkers (1986 a–c; 1988 a–c; 1989a–c; 1991b) supported more and more the opinion that the relation between schizoaffective and affective disorders is stronger than the relation between schizoaffective and schizophrenic disorders.

Using larger sample sizes and more sophisticated statistical methods, Astrup and Noreik (1966) published a series of reports from 1957 to 1966 in which they analyzed the outcome of more than 1200 cases of schizophrenia. Those schizophrenics who recovered (n = 131) instead of deteriorating (n = 416) were the ones who showed affective symptoms: elation, psychomotor agitation, flight of ideas, mood swings. Here, the affinity of the illness with affective disorder was seen as central.

Applying Schneider’s first-rank symptoms along with Bleuler’s criteria to specify the schizophrenic dimension within schizoaffective disorder, Spitzer et al. (1978) wrote the following rules for the diagnosis: i.e the research diagnostic criteria (RDC) for schizoaffective disorder (manic/depressive subtypes). These included the full manic or depressive syndrome and at least one of the following symptoms suggestive of schizophrenia: delusions of being controlled or of thought broadcasting, insertion or withdrawal; non-affective hallucinations for several days straight or intermittently throughout a week; auditory hallucinations (a voice doing a running commentary on the subject or two or more voices conversing); more than a week of delusions or hallucinations without accompanying prominent depressive or manic symptoms; more than a week of marked formal thought disorder with blunted or inappropriate affect or delusions or hallucinations; or grossly disorganized behavior, but no prominent manic symptoms. In addition, the symptoms were to have a duration of at least one week, with a temporal overlap of affective with schizophrenia-like symptoms.
In the nineteen seventies period of the twentieth century, it became common for the clinical diagnosis of schizoaffective disorder to require both affective and schizophrenic symptoms, combined with a minimum duration. Welner et al. (1977), Kendell and Gourlay (1970), Angst et al. (1979), Mendlewicz et al. (1980), Perris (1966), and Tsuang et al. (1976) provide examples.

According to Welner et al. (1977), there should be enough affective symptoms to make the diagnosis of schizophrenia unlikely, yet not necessarily enough to meet the criteria for schizophrenia: sufficiently severe thought and behavior disorders, and at least one of the following: acute onset, episodic course, or confusion; and psychosis not associated with alcohol, drug abuse, or known organic brain disease. The findings of Welner et al. based on these criteria (1977; 1979) did not support the traditional association of schizoaffective disorder and good prognosis. Over 70% of 114 patients diagnosed as suffering from schizoaffective or related psychoses had a chronic course of illness, and over 80% of these chronic cases deteriorated. A related family study of 27 relatives with psychotic symptoms showed that 20 probands with both affective and schizophrenic symptoms also had a chronic course of illness. It must be noted, however, that neither a minimum duration of symptoms nor a complete remission of symptoms between episodes was required for the selection of these probands. A study by Himmelhoch et al. (1981) which supports these findings similarly neglected to require a minimum duration of symptoms.

In the view of Kendell and Gourlay (1970), either schizophrenia or paranoid psychosis must first be present. For schizophrenia, one of the core symptoms (thought insertion, withdrawal, broadcasting, echoes, voices, delusions of control) or two objective signs, either behavioral (mannerisms, posturing, stereotypes, catatonic phenomena, or behavior suggesting hallucinations) or affective (suspicion, perplexity, blunting, or incongruity) or relating to speech (neologisms, incoherence, non-social speech) must be present. For paranoia, a delusion involving the external world, such as delusions of influence, persecution, reference, misinterpretation, etc., must be present and must be persistent and preoccupying; the patient must show conviction. Second, either depression or mania must be present. For depression, four items from a list of 16 must be fully rated (sadness, hopelessness, suicidal intent, loss of interest, inferiority, pathologic guilt, hypochondriacal delusions, nihilistic delusions, insomnia, muddled thoughts or poor concentration, morning depression, and loss of appetite, libido or emotions), and three signs must be evident (observed sadness, agitation, retardation). For mania, three fully rated items from the following list of five symptoms (euphoria, racing thoughts, tirelessness, delusions of special powers, delusions of grandiose identity) and seven signs (over-activity, distractibility, irreverent behavior, embarrassing behavior, hypomanic affect, pressure of speech, flight of ideas) must be present.
In Angst’s definition, as well as in Welner’s, both affective and schizophrenic symptoms should be present, each strong enough to make the opposite diagnosis unlikely. Patients should show a tendency towards remission with no marked defect, yet also towards recurrence. Angst studied the morbidity risk for schizophrenia among 1000 first-degree relatives of 150 schizoaffectives selected by these criteria. He found the risk to be 5.26%, compared with a risk of affective disorder of 6.7%. Full remission among schizoaffectives was less common (43%) than among those with bipolar disorders (73%) (Angst et al., 1979). If Welner’s findings suggest that schizoaffective disorder bears a relationship to schizophrenia by virtue of being similarly chronic, Angst’s findings rather suggest that schizoaffective disorder is equally related to pure schizophrenic and mood disorder.

The criteria of Mendlewicz (1980) include episodic affective syndromes of the manic or depressive type and at least one schizophrenic episode not concurrent with an affective syndrome.

The concept of atypical schizophrenia according to Tsuang et al. (1976) relies on a diagnosis of schizophrenia essentially based on the Feighner criteria, but with either short duration or the possibility of another diagnosis and either a previous remitting illness or affective symptoms at the time of admission. Tsuang et al. (1986) presented a detailed example of the application of similar criteria for the purpose of subtyping schizoaffective disorder.

Despite the impression of catalogued precision which some of the above definitions gave and certain themes which recur among them, a number of them have been shown not to select the same group of patients. In 1979, Brockington and Leff reported the results of an objective comparison for some of these criteria. They tested the validity of eight different sets of criteria for schizoaffective disorder, including the CATEGO System (Wing et al., 1974), Kendell’s criteria (1970), Kasanin’s criteria (1933), Stephens’s criteria for “good prognosis schizophrenia” (Stephens et al., 1966), the study criteria of Welner, and Spitzer’s RDC for schizoaffective disorders (Spitzer et al., 1978). Based on information from blind interviews of 119 psychotic patients, who met at least one of the definitions, the researchers found a very low level of concordance between the eight different definitions of schizoaffective disorder compared with criteria for schizophrenia and affective disorder. One weakness of this study was the fact that it eliminated any criteria based upon longitudinal information. The authors concluded that it is highly unlikely that the diagnostic concept of schizoaffective disorder currently in use corresponds to anything coherent in nature.

Later research by Brockington et al. (1980a–b) further undermined the concept of schizoaffective disorder. Their study of 32 patients meeting criteria for “schizomanic” psychosis made them conclude that, in terms of response to lithium treatment and overall outcome, most of their patients could be re-classified
as manic. They subsequently analyzed family history, treatment response, and outcome for 76 patients who showed signs both of depression and of schizophrenia or paranoia. These patients presented a more intransigent problem. Many of them were ultimately re-diagnosed as schizophrenic or bipolar, but 20 eluded all attempts at reclassification. This might suggest a continuum model of psychiatric illness or the heterogeneity of schizoaffective disorder, but in any case does nothing to lessen confusion in the field. Some researchers have done away with the traditional categories altogether. Vaillant (1962) found six variables which yielded 82% accurate prognoses. These were: psychotic depressive heredity, symptoms suggesting a depressive psychosis, onset within six months before the fully developed illness, presence of precipitating factors, absence of schizoid personality before onset, and confusion or disorientation during the acute episode.

In a 1964 study, he added a seventh variable, the fear of death. Individual case histories were rated on a scale of 0–7; a rating above 4 predicted good outcome and below 4 predicted bad outcome. This placing of cases on a continuum helps to offset the problem that, once a diagnostic scheme is in place, the labels associated with that diagnostic scheme can influence the observation of patients and the conceptualization of their illnesses in a biased manner. The continuum concept eliminated the need to create a new category of illness or a residual category in order to classify patients with schizoaffective features. However, diagnoses may then multiply without limit, and end up in conceptual chaos. The conceptual chaos has to be minimized also in regard to the relationship of schizoaffective psychoses to other “atypical” psychoses. Sometimes, the terms “cycloid psychosis,” “psychogenic” or “reactive psychosis”, and the French term “bouffée délirante” are used synonymously with schizoaffective psychosis (Marneros and Pillmann, 2005). However, there are very important differences between these psychoses – later called “acute and transient psychotic disorder” – and the psychopathologic picture of schizoaffective psychoses, so that they cannot be assumed to be identical (Perris, 1974; 1986; Pichot, 1986 and Strömgren, 1986; Marneros and Pillmann, 2005).

One of the most voluminous and comprehensive studies of the schizoaffective area is the Cologne Study, carried out by Marneros, Deister and Rohde and published in a German monograph with an extensive English summary in 1991 (Marneros et al., 1991b). The Cologne Study is a naturalistic study comparing 402 patients with schizoaffective, affective, and schizophrenic disorders with an average illness duration of more than 25 years. The Cologne Study distinguishes between “episodes” (which is a cross-sectional diagnosis [Marneros et al., 1991b] – and “illnesses or disorders” [which is a longitudinal diagnosis]). The Cologne Study showed an intermediate position of schizoaffective disorders between schizophrenia and mood disorders on almost all investigated levels (premorbid, family, social,
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personality, course and longitudinal outcome). It showed also that schizoaffective disorders have a very strong relation to mood disorders and they have to be distinguished into unipolar and bipolar forms (Marneros et al., 1990a–c).

The ICD and DSM evolution: their strengths and weaknesses

As Pichot (1986) pointed out, the official American history of the disorder “schizoaffective” can be followed in the successive editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) of the American Psychiatric Association (APA). DSM-I (APA, 1952) describes the “schizoaffective type” among the “schizophrenic reactions.” The criteria used in DSM-I are different from Kasanin’s original description: no mention is made of sudden onset, shortness of episode, or complete recovery.

DSM-II (APA, 1968) included the category “schizophrenia, schizoaffective type.” The definition, however, had become brief and non-committal: “Patients showing a mixture of schizophrenic symptoms and pronounced elation and depression.” The ICD-8, published in the same year, contained the same category.

In 1978, the Task Force on Nomenclature and Classification of the APA published the draft of DSM-III. It included a special category, schizoaffective disorders, completely distinct from schizophrenic disorders. The criteria proposed as essential were “a depressive or manic syndrome . . . that preceded or develops concurrently with certain psychotic symptoms thought to be incompatible with a purely affective disorder”. The DMS-III draft stated, “The term schizoaffective has been used in many different ways. . . . At the present time there is a controversy as to whether this disorder represents a variant of Affective Disorder of Schizophrenia, a third independent nosological entity, or part of a continuum between pure Affective Disorder and pure Schizophrenia”. The separate listing is justified by “the accumulated evidence that individuals with a mixture of ‘affective’ and ‘schizophrenic’ symptoms, as compared with individuals diagnosed as having schizophrenia, have a better prognosis, a tendency towards acute onset and resolution, more likely recovery to premorbid level of functioning, and an absence of a prevalence increase of schizophrenia among family members . . .”

Two years later, in the final printed edition of DSM-III (APA, 1980), the category had practically disappeared. The manic episode and the major depressive episode now included cases with “mood-incongruent psychotic features” which, in the draft, would have belonged to the schizoaffective disorders. It is true that DSM-III has formally retained a category called schizoaffective disorders but, being without diagnostic criteria, it was considered as a residual class “for those instances in which the clinician is unable to make a differential diagnosis between Affective Disorders and either Schizophreniform Disorder or Schizophrenia.”
A new category, schizophreniform disorder, appears. As Pichot (1986) pointed out, this category is very similar to Kasanin’s original schizoaffective psychosis as far as the evolution is concerned: “The duration . . . is less than six months . . . [there is] a tendency towards acute onset and resolution . . . recovery to premorbid levels of functioning,” but the symptomatic criteria are those of schizophrenia, with the exception of “a greater likelihood of emotional turmoil and confusion.” No mention of affective symptoms is made (Pichot, 1986).

In DSM-III-R, published in 1987, schizoaffective disorders were born again – this time classified independently from both schizophrenia and affective disorders in the category “psychotic disorders not elsewhere classified” and with their own diagnostic criteria as well as with subtypes, namely bipolar type and depressive type. In DSM-IV, published in 1994, schizoaffective disorders belong to the category “other psychotic disorders” with almost the same diagnostic criteria and the same subtypes as in DSM-III-R. This time the mixed bipolar symptomatology is also recognized.

ICD-9 (1976) continued the tradition of ICD-8 (1968). In ICD-10 (1991), after bouncing like a ping-pong ball during successive draft publications, schizoaffective disorders landed in a category of their own within schizophrenia and delusional disorders, with extensive description and with five subcategories:

- Schizoaffective disorder, manic type
- Schizoaffective disorder, depressive type
- Schizoaffective disorder, mixed type
- Other schizoaffective disorders
- Schizoaffective disorders, unspecified

The evaluation of the concept and the definition of schizoaffective disorders continue. Many aspects remain to be clarified, many questions still require answers. Most diagnostic systems only recognized the concurrent form of schizoaffective disorders, not the sequential ones. But operational research showed no differences in any investigated dimension between concurrent and sequential schizoaffective disorders (Marneros et al., 1988a–c; 1991b).

We lost valuable time ignoring the sequential type of schizoaffective disorders. Nevertheless, the ongoing evolution of concepts and definitions of schizoaffective disorder also means continuing uncertainty. The question “What are the schizoaffective disorders?” remains unanswered.

Schizoaffective disorders present in both DSM-IV and ICD-10 (APA, 1994; WHO, 1992) as unipolar or bipolar forms in a way similar to mood disorders (Marneros et al., 1989a–b, e; Marneros et al., 1990 a–c; Marneros et al., 2000). However, there are essential differences between DSM-IV and ICD-10 (Marneros and Goodwin, 2005b). While DSM-IV defines two subtypes based on longitudinal course, namely