Schizoaffective Disorder: Concept and Reality

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Abstract

A wide variety of concepts have been proposed to account for schizoaffective psychoses. Presenting a mixture of schizophrenic and affective symptoms, these psychoses have long defied classification in the usual scheme of the two major diagnostic categories, schizophrenia and major affective disorder. Empirical findings are often contradictory, and have sometimes supported the classification of schizoaffective disorder with schizophrenia, and, more recently, with major affective disorders. An alternative hypothesis is that schizoaffective disorder is fundamentally heterogeneous, and that research efforts should be directed toward the identification of homogeneous subtypes. To illustrate the latter research strategy, we describe our current research program of long-term followup and family studies of patients with schizoaffective psychoses and other atypical psychoses. Extensive data have been obtained using blind, structured psychiatric interviews with probands after 30 to 40 years of followup, and with their first degree relatives. In the same way, followup and family data were obtained for patients who met research criteria for schizophrenia, mania, and depression, and for matched surgical controls. By comparing these groups of "typical" psychotic patients with the schizoaffective patients, we can select homogeneous subgroups of schizoaffective patients and analyze their characteristics to refine clinical and research criteria for the differential diagnosis of schizoaffective subtypes.

The purpose of this article is to discuss diagnostic concepts of schizoaffective disorder and the relation of those concepts to the reality of psychotic disorder in patients who have schizoaffective features. This topic is of interest for several reasons. First, it addresses the clinically important question of the appropriate diagnosis and treatment of substantial numbers of "atypical" psychotic patients, i.e., those who do not unambiguously satisfy diagnostic criteria for schizophrenia or major affective disorder. In particular, we are concerned here with the occurrence in individuals of both schizophrenic and affective features, e.g., delusions, hallucinations, thought disorder, or bizarre behavior, accompanied by striking manic or depressive symptomatology, acute onset, and good recovery.

Secondly, the issue of the validity of the concept of schizoaffective disorder lies at the heart of the major enduring controversy in modern psychiatry: the classification of psychotic patients and, specifically, the differential diagnosis of schizophrenia from bipolar disorder (manic-depression) and major depression.

In view of the daunting complexity of these problems and the relatively primitive state of empirical research, we argue throughout this review for the continuing need to consider all relevant factors in order to avoid premature and oversimplified conclusions. Following a discussion of diagnostic concepts related to the issue of schizoaffective disorder, we selectively review the empirical support for various diagnostic models, and describe recent research trends in this field. We also present our own reasons for adopting a research strategy based on a search
The Concept of Schizoaffective Disorder

Although the introduction of the term "schizoaffective psychosis" can be traced back 50 years to an influential presentation by Kasanin (1933), concern with forms of psychosis showing mixed features of schizophrenia and affective disorders has been a prominent fixture of psychiatric discourse for far longer, due to the fundamental importance of the differential diagnosis of schizophrenia and manic-depression. As Kasanin (1933, p. 99) himself acknowledged after characterizing schizoaffective patients, "Bleuler many years ago recognized such cases." It is instructive to consider Bleuler's position in some detail because of its historical importance leading to the concept of schizoaffective disorder as a form of schizophrenia.

Bleuler (1911/1950) devoted considerable attention to the differential diagnosis of schizophrenia and "manic-depressive psychosis" and, in doing so, discussed the conjunction of schizophrenia and manic-depressive symptoms. His theoretical position was that all manic-depressive symptoms can also occur in schizophrenia, and furthermore, that "hallucinations and delusions are partial phenomena of the most varied diseases." Hence the presence of these symptoms "is often helpful in making the diagnosis of psychosis, but not in diagnosing the presence of schizophrenia" (p. 294).

To make the differential diagnosis, Bleuler relied on the presence or absence of specific schizophrenic symptoms, namely, those "fundamental" symptoms that defined the schizophrenic splitting of cognition from emotion and behavior: formal thought disorder, flat or blunted affect, autistic tendencies, and ambivalence. In view of recent concern with overreliance on nonspecific schizophrenic symptoms for purposes of diagnosis (e.g., Pope and Lipinski 1978), it is instructive to note the theoretical distinction that Bleuler made between these "fundamental symptoms" and less specific "accessory" symptoms such as delusions and hallucinations. In practice, however, Bleuler appears to have relied heavily on accessory as well as fundamental symptoms for differential diagnosis. Thus, although he acknowledged the occurrence of delusional states in manic-depression, and was careful to distinguish between formal thought disorder in schizophrenia compared to mania (schizophrenic "incoherence" vs. manic "flight of ideas") and in schizophrenia compared to depression (schizophrenic "blocking" vs. depressive "inhibition"), he believed that many cases of "melancholia and mania," "especially those with hallucinatory mania or melancholia, or with manic or melancholic delusions, respectively, belong to schizophrenia" (p. 287).

Differences in the course of the illness were also used by Bleuler to distinguish between schizophrenia (typically leading to deterioration) and manic-depression (with almost full recovery between episodes). However, atypical cases were also possible: "The periodic or cyclic course may be absent in manic-depressive psychosis whereas, on the other hand, it may occur in schizophrenia" (p. 311). The decisive factors in such cases were again the presence or absence of "distinct signs of schizophrenia."

In summary, Bleuler's basic position was that the combination of schizophrenic and manic-depressive features usually represented schizophrenia, and that the presence of "fundamental" schizophrenic symptoms unambiguously indicated cases of schizophrenia, regardless of the extent of affective symptomatology.

In contrast to Bleuler, Kasanin's (1933) concern in describing schizoaffective patients was to delineate homogeneous subgroups of psychotic patients, and in particular, to differentiate a specific type of atypical case from a homogeneous group of "constitutional schizophrenics." As such, his concept of "schizoaffective psychosis" was primarily descriptive and does not clearly indicate the relation of this syndrome to schizophrenia and manic-depression.

However, by virtue of describing a distinct homogeneous group of psychotic patients, his concept leads readily to the concept of a diagnostic entity different from schizophrenia and from manic-depression, but sharing features of both.

The primary value of Kasanin's 1933 report was his precise description of what he believed to be a homogeneous group of patients, his isolation of the primary features, and his felicitous choice of the term "schizoaffective" to label this syndrome by highlighting the atypical yet characteristic blending of schizophrenic and affective symptoms. Other defining features included:

- Ages 20-39;
- Usually a history of a previous attack in late adolescence;
- Normal premorbid personality;
- Good social and work adjustment;
- Very sudden onset in a setting of marked emotional turmoil with a distortion of the outside world and presence of false sensory impressions in some cases;
• Definite and specific environmental stress;
• Absence of any passivity or withdrawal;
• Duration of a few weeks or months and followed by recovery.

Not surprisingly, subsequent investigators have not always been content to adopt Kasanin's terminology or definition, but have proposed various terms and definitions in line with their own clinical interests and theoretical orientations. Nor did that process begin after Kasanin. Reports by Kasanin (1933) and other investigators as far back as Bell (1849) have been described by Vaillant (1965) as "the efforts of psychiatry to rename the recovered schizophrenic." Among the 16 eponyms that Vaillant lists are "mixed conditions of manic-depressive insanity" (Kraepelin 1913), "hysterical twilight state" (Bleuler 1924), "schizophreniform state" (Langfeldt 1937), and "cycloid psychoses" (Leonhard 1961). Procci (1976) compiled a similar list, updated to include Vaillant's (1965) own "remitting schizophrenia," as well as "recovered schizophrenics" (Stephens, Astrup, and Mangrum 1966), "good prognosis schizophrenia" (Fowler et al. 1972), and "reactive psychoses" (McCabe and Stromgren 1975).

In the face of this profusion of studies, systematic progress toward understanding schizoaffective psychoses has been slowed by a lack of agreement on diagnostic terminology, and the resultant difficulty of comparing study samples and results, and of replicating previous findings. A particular source of confusion is the widespread use of the term "schizoaffective" to cover a variety of samples, usually without specific diagnostic criteria. This situation persists in *DSM-III* (American Psychiatric Association 1980), with its emphasis on the inclusion of patients with mixed schizophrenic and affective symptoms within the diagnostic categories of "schizophrenia with a superimposed atypical affective disorder" and "major depression or bipolar disorder with mood-congruent or mood-incongruent psychotic features." "Schizoaffective disorder" survives only as a diagnostic category of last resort, and is defined as psychotic illness with a mixture of schizophrenia and affective symptoms that fails to satisfy diagnostic criteria for schizophrenia, major affective disorders, or schizophreniform disorder. In contrast, the Research Diagnostic Criteria (RDC) of Spitzer, Endicott, and Robins (1978) include specific diagnostic criteria for schizoaffective disorder and even for manic and depressed subtypes.

That both *DSM-III* and RDC retain the term "schizoaffective" emphasizes the dominant concern with the combination of schizophrenic and affective features, whether they occur concurrently or in distinct episodes. The choice of terminology is important because diagnostic labels serve as convenient highly abbreviated descriptions. For example, "dementia praecox" emphasized early onset and deterioration (poor prognosis); "schizophrenia" emphasizes the splitting (lack of coordination) of the mental processes of cognition, emotion, and behavior; and "affective disorder" emphasizes mood disruption. The amount of distortion caused by such abbreviated description is offset, one hopes, by selection of the most significant or salient features. Fortunately, the recent widespread adoption of operational definitions using specific diagnostic criteria has reduced the import of diagnostic terminology, although the choice of terminology still plays a major role in our thinking and discourse.

Faced with the mounting confusion attributable largely to conceptual vagueness and the lack of uniform diagnostic criteria, several investigators have attempted directly to clarify the diagnostic puzzle of schizoaffective disorder. Vaillant (1965) systematically compared the common features observed by his selected list of 16 studies of remitting schizophrenics. There was good agreement across most studies about the salient features, which included:

• An acute picture resembling schizophrenia but with symptoms of psychotic depression;
• Acute onset;
• Confusion or disorientation during the acute onset;
• Good premorbid adjustment;
• A clear precipitating event; and
• Remission to the best premorbid level of adjustment.

Comparison with Kasanin's (1933) list of defining features for schizoaffective psychoses (given above) shows a close correspondence.

Procci (1976) updated Vaillant's comparison and found continued good agreement across studies on the salient features of patients who are "neither clearly schizophrenic nor clearly bipolar affective." In addition to the features listed above, Procci's review found evidence that such patients characteristically have a family history of depression (also stressed by Vaillant 1965, 1978) and psychomotor excitation (hypomanic features). Having isolated a consistent subtype, Procci proceeded to review the response to lithium carbonate therapy, followup studies, and family studies of schizoaffective patients. He concluded that schizoaffective psychosis encompasses a
heterogeneous group of disorders, but that the relatively homogeneous group defined above probably represents "a variant of affective disorder or an independent entity bearing a similarity to affective disorder" (p. 176). This conception of schizoaffective disorder corresponds nicely with Kasanin's (1933) emphasis on homogeneous subgroups of psychotic patients. If schizoaffective disorder is fundamentally heterogeneous, it could be that several diagnostic concepts will be needed to describe homogeneous subgroups of schizoaffective patients. Mention has already been made of the manic and depressive subtypes of schizoaffective disorder described by the RDC. Tsuang (1979) hypothesized that there are three distinct schizoaffective subtypes: a schizophrenic subtype closely related to schizophrenia, an affective subtype closely related to affective disorder, and an undifferentiated subtype that is distinct from both schizophrenia and affective disorder. A fourth possible subtype, of unknown significance at present, would represent the more-or-less random occurrence of schizophrenia and affective disorder in the same person, corresponding to Bleuler's "mixed forms of manic-depressive psychosis and schizophrenia," e.g., "manic-depressive attacks released by schizophrenia" (Bleuler 1950, p. 269).

A relatively recent and highly influential conception of schizoaffective disorder is that it represents (in many or most cases) a form of affective disorder, primarily bipolar affective disorder. This viewpoint has been forcefully argued in critical reviews by Ollerenshaw (1973) and by Pope and Lipinski (1978). Central to this argument is the nonspecificity of schizophrenic symptoms, contrasted with the predictive utility of affective symptoms. We will discuss the empirical support for these points below. We merely note here that this conception represents a striking reversal from the Bleulerian position that patients with schizophrenic and affective symptoms are probably schizophrenic. If the more recent position is correct, it will mark a major landshift in psychiatric thought.

Nevertheless, the concept of schizoaffective disorder as a form of affective disorder agrees with the Kraepelian (and Bleulerian) two-entities tradition—that schizophrenia and affective disorder are the two primary and distinct forms of psychosis. This tradition has also been challenged by the view that there is a continuum or spectrum of psychotic illness running from schizophrenia to affective disorder (Beck 1967). In this view, the mixture of schizophrenic and affective features does not represent a distinct diagnostic entity, but rather an intermediate region of the continuum where schizophrenic psychosis shades into affective psychosis. In contrast to the two-entities tradition, for which the existence of schizoaffective patients poses a major puzzle and something of an embarrassment, schizoaffective syndromes fit naturally into the schema of a continuum model. An interesting variant of the continuum model, leading to a similar conception of schizoaffective disorder as an intermediate form of psychosis, is the hierarchical model of Foulds and Bedford (1975).

We close this section with mention of an empirical comparison by Brockington and Leff (1979) of eight alternative definitions of schizoaffective psychosis and related syndromes, including the definitions of Kasanin (1933), Stephens, Astrup, and Mangrum (1966), Welner, Croughan, and Robins (1974), the Catego system (Wing, Cooper, and Sartorius 1974), and the RDC. In general, the agreement across definitions was low. Values of Kappa (a measure of concordance corrected for chance agreement) ranged from − .03 to .50 (for Kasanin vs. Stephens), and the mean value of Kappa across the diagnostic comparisons was .19 (or, less conservatively, .27). In view of the generally acceptable reliability of most of these definitions, the authors attributed this low concordance to substantive disagreement about the defining characteristics of schizoaffective disorder. This contrasts sharply with the conclusions of Vaillant (1965) and Procci (1976) that studies of schizoaffective-like patients have usually studied similar individuals with a readily identifiable syndrome.

In this section, we have reviewed some of the major concepts of schizoaffective disorder, and pointed out several areas of contention. Unfortunately, as demonstrated by Brockington and Leff (1979), there is still considerable disagreement about the validity of different concepts of schizoaffective disorder. What makes the issue so difficult to resolve is that each concept, by virtue of being a diagnostic concept, entails unique diagnostic criteria that result in selecting patients for study who differ to some degree from patients defined by an alternative concept. Hence, reports based on different diagnostic concepts inevitably produce different findings. The only apparent way out of this "unnerving circularity" is through "a continuous process whereby increasingly refined diagnoses allow more definitive studies of inheritance, outcome, response to treatment, etc... which in turn shape diagnostic concepts" (Brockington and Leff 1979, p. 97). To aid in this process, we now survey empirical findings relevant to
the major concepts of schizoaffective disorder.

**Empirical Studies of Schizoaffective Disorder**

**Schizoaffective Disorder as a Form of Schizophrenia.** Historically, this concept has been based largely on the Bleulerian position that certain schizophrenic symptoms have pathognomonic importance for the differential diagnosis of schizophrenia, whereas affective symptoms are nonspecific (Bleuler 1950). Uncritical application of this position evidently resulted in the overdiagnosis of schizophrenia in America and a tendency to lump any patients with even relatively nonspecific schizophrenic symptoms (such as delusions and hallucinations) together with more typical cases of schizophrenia (Pope and Lipinski 1978). Though a trend away from viewing schizoaffective disorder as a subtype of schizophrenia is discernible in the recent literature on the subject, Croughan, Welner, Robins, and associates (Croughan, Welner, and Robins 1974; Welner et al. 1977; Welner, Welner, and Fishman 1979), in a series of articles reporting the findings arising from their extensive study of schizoaffective patients, conclude that schizoaffective disorder is an expression of schizophrenia and does not merit the status of a distinct diagnostic entity.

Historically, a commonplace of schizoaffective research has been the observation that patients presenting symptoms of both schizophrenia and affective disorder are more likely to recover than those presenting schizophrenic symptoms alone (Vaillant 1965; Procci 1976; Pope and Lipinski 1978). The findings of Welner et al. (1977) do not support this traditional association of schizoaffective disorder and good prognosis. In their study, over 70 percent of the 114 patients diagnosed as suffering from schizoaffective or related psychoses had a chronic course of illness, and over 80 percent of these chronic cases deteriorated. This is not an isolated finding, but agrees with several recent longitudinal studies of good prognosis or remitting schizophrenics that have shown little or no prognostic significance for affective symptoms in patients with marked schizophrenic symptomatology (Hawk, Carpenter, and Strauss 1975; Vaillant 1978; Gift et al. 1980). Since Kraepelin’s time, a chronic, deteriorating course has been considered a sign of schizophrenia. Thus, Welner et al. (1977) conclude that “when schizoaffective illness is used to describe a psychosis whose cardinal symptoms are both schizophrenic and affective, the psychosis should be regarded as schizophrenia” (p. 420). In a subsequent article, Welner, Welner, and Fishman (1979) attempted to validate this finding in a family study of 20 probands whose first degree relatives had a history or presence of affective or psychotic symptoms. Twenty-seven of the 30 relatives who had psychotic symptoms also had a chronic deteriorating course of illness which was consistent with a diagnosis of schizophrenia. The authors recommended that patients presenting a confusing admixture of acute schizophrenic and affective symptoms be labeled “undiagnosed” rather than “schizoaffective” because there is insufficient evidence for the validity of schizoaffective disorder as a distinct diagnostic entity.

Recently, Himmelhoch et al. (1981) published a report coinciding with the conclusions of Welner et al. at a number of significant points. After 748 patients were examined with rigorous diagnostic criteria, only 39 were identified as schizoaffective. The authors concluded that schizoaffective disorder, when defined by stringent longitudinal standards, is a rare diagnosis. The diagnostic criteria used by Himmelhoch et al. are similar to, but not identical with, those of Welner et al., with the most significant difference being the former group’s requirement of inter-episodic thought disorder. Among patients who suffered thought disorders between acute psychotic episodes marked by prominent affective features, a significant difference was noted between patients labeled “schizoaffective” and those labeled “affective” on clinical, demographic, and prognostic variables. Clinically, schizoaffective patients were less likely than affective patients to abuse drugs. Based on demographic information, schizoaffective patients were more likely than affective patients never to have married, and, as for prognosis, schizoaffective patients were more likely than affective patients to relapse. These data suggested a similarity between schizoaffective disorder and schizophrenia. However, Himmelhoch et al. were not willing to go as far as Welner et al. and dismiss schizoaffective disorder as a useful diagnostic entity. They concluded that although it may be a category only rarely invoked, “schizoaffective” retains its diagnostic function by pointing to an affective element that is not part of our usual conception of schizophrenia.

**Schizoaffective Disorder as a Form of Affective Disorder.** Beginning in the late 1960s, a number of recent studies have argued that schizoaffective disorder is actually misdiagnosed affective disorder. Stephens, Astrup, and Mangrum (1966) eschewed the complexities of diagnosing schizoaffective disorder as a subtype of...
schizophrenia, in favor of a simpler rating on a prognostic scale. From studies of “good prognosis schizophrenics,” McCabe et al. (1972) and Fowler et al. (1972) suggested that the disorder they studied might be a variant of affective disorder rather than a subtype of schizophrenia. Similar conclusions were reached by Clayton, Rodin, and Winokur (1968), based on family history data. McCabe and Cadoret (1976) also noticed a clear dissimilarity between schizoaffective disorder and schizophrenia in their review article, which examined age-corrected morbidity risks for the first degree relatives of patients with atypical psychoses. The studies they analyzed consistently reported that relatives of patients with atypical psychoses are more likely to suffer from remitting psychoses than from nonremitting psychoses. In their summary McCabe and Cadoret maintained that “the genetic evidence would suggest that the relationship of atypical psychoses to schizophrenia is minor” (p. 352).

A number of recent studies have suggested that in many cases, schizoaffective patients would be more accurately classified as having a major affective disorder. These studies view “schizoaffective disorder” as a misnomer, as a label inappropriately applied to a purely affective disorder because of confusing symptomatology. Readers of these studies are frequently reminded that acute episodes of mania sometimes manifest symptoms suggestive of schizophrenia. The well-documented tradition of giving precedence to schizophrenic symptoms, especially in the United States, explains why a large number of difficult-to-diagnose cases of bipolar affective disorder may have been falsely labeled “schizoaffective.”

Sovner and McHugh (1976) concluded from a chart followup of 27 schizoaffective patients that bipolar patients are sometimes mistakenly diagnosed as schizoaffective because of the time-honored practice of giving more weight to schizophrenic symptoms when the clinical picture is ambiguous. Abrams and Taylor (1976), using the RDC, were unable to find any significant difference between groups of patients with mania and schizoaffective disorder, manic type, compared for symptoms, demographic characteristics, individual or family history, or treatment response. Brockington, Wainwright, and Kendell (1980) likewise observed close similarities between “schizomania” and “manic-depressive psychosis” in a 1- to 4-year followup study of 32 “schizomanic” patients. They concluded that consideration should be given to expanding the definition of typical mania to encompass patients whose manic symptomatology is complicated by delusions, hallucinations, and passivity phenomena. Pope and Lipinski (1978), in an overview of the use of schizophrenic symptoms in diagnosis, argued that the subordination of schizoaffective disorder to schizophrenia is the result of a misguided tendency to attach the label “schizophrenic” to any disorder which manifests hallucinations, delusions, or emotional blunting, despite the fact that one or more of these can appear in cases of affective disorder. They appeal to phenomenologic studies, prognostic studies, family history studies, treatment-response studies, and combination studies to buttress their conclusion that “the entire range of ‘schizophrenic’ symptoms is recorded, not in a few cases of MDI [manic-depressive illness], but in about 20 percent to 50 percent of both manic and depressed patients” (p. 813).

Hence, although they do not rule out the possibility of a distinct disorder separate from schizophrenia and affective disorder, Pope and Lipinski argue that the data which point in this direction can be more convincingly and economically explained by assuming that many, if not all, cases labeled “schizoaffective” are actually cases of affective disorder.

However, not all studies which posit a close relationship between schizoaffective and affective disorder lead to the conclusion that the two disorders should be collapsed into one. Tsuang, Dempsey, and Rauscher (1976) and Tsuang and Dempsey (1979) examined a group of 85 schizoaffective patients from a series of 310 consecutive “atypical” schizophrenic admissions at the University of Iowa Psychiatric Hospital between 1934 and 1944. All these patients received hospital diagnoses of schizophrenia, but failed to meet the Washington University diagnostic criteria for schizophrenia (Feighner et al. 1972) because of short duration of symptoms or the presence of affective symptoms at admission. Ninety-eight percent of the 85 schizoaffective patients had depressive symptoms (75 percent had four or more depressive symptoms), and 80 percent had manic symptoms (58 percent had three or more manic symptoms) (Tsuang, Dempsey, and Rauscher 1976). The schizoaffective patients were compared with 200 schizophrenics and 325 affective disorder patients (100 bipolar, 225 unipolar) selected according to the Washington University diagnostic criteria. At admission the schizoaffective patients most resembled the bipolar group except for a significantly higher proportion of precipitants and an earlier age of onset in the schizoaffective group. At followup 30 to 40 years later, the schizoaffective group fared significantly better than the group of schizophrenics, but signif-
Significantly worse than the affective disorder groups. Taken together, these findings indicate that schizoaffective disorder is in some ways more closely related to affective disorder than to schizophrenia and should clearly be excluded from studies of schizophrenia. However, the complexity of the overall picture also argues against a simple reclassification of schizoaffective disorder as a form of affective disorder.

Schizoaffective Disorder as a Distinct or Heterogeneous Illness. Leonhard (1961) described three acute onset psychoses with good prognosis under the heading of "cycloid" psychoses, which he claimed were neither schizophrenic nor affective disorders, but constituted a distinct diagnostic entity. The work of other investigators has subsequently supported this conclusion. Kaj (1967) and Walinder (1972) reported two families with a history of schizoaffective psychosis. The main characteristics of relatives with this psychosis were a strong affective component—predominantly depression, swings in mood between elation and despondency, some paranoid delusions, confusion, and an acute, sometimes sudden onset and complete recovery. More recently, Perris (1974) used Leonhard's classificatory system and concluded that the cycloid psychoses do, in fact, represent a distinct nosological entity based on the outcome of 60 patients. These patients were characterized by acute onset, periodic recurrence, termination free from residual defects, and an array of other illness-related factors. McCabe (1975) examined 40 patients from Denmark who had psychoses specifically related to a precipitating stress according to the criteria of Stromgren (1968), and concluded that these patients could be distinguished as a third functional psychosis after manic-depressive psychosis and schizophrenia.

Mitsuda (1965, 1967, 1974) focused attention on the relationship between "atypical psychosis" and epilepsy. Mitsuda pointed out that atypical psychosis, with both schizophrenic and affective features, carries a paroxysmal or "ictal" stamp, and is nearly always characterized by disorders of consciousness. He also noted a higher incidence of epilepsy rather than schizophrenia or manic-depressive psychosis among the families in his study. Mitsuda argued that "atypical psychosis" is a distinct nosological entity which could be transmitted as a dominant or as a recessive trait. Since there is no clear evidence of the mode of inheritance, however, a cautious attitude should be adopted toward these results.

Studies of psychiatric illness in relatives of schizoaffective patients provide a useful source of information about distinctiveness of schizoaffective disorder. If schizoaffective disorder is genetically distinct, we would expect to find an increased risk of schizoaffective disorder in families of schizoaffective patients compared to families of patients with schizophrenia or major affective disorder. We would also expect to find less schizophrenia in relatives of schizoaffective patients than in relatives of schizophrenic patients, and less affective disorder in relatives of schizoaffective patients than in relatives of patients with affective disorders.

Recently, a number of studies have been made of psychiatric illness in relatives of schizoaffective patients. Abrams (1984, this volume) reviewed this topic in detail and concluded that the empirical data provided by these recent studies do not support the status of schizoaffective disorder as a separate and distinct diagnostic entity. The reader is referred to Abrams' article for a detailed discussion of this research. The general pattern is that schizoaffective disorder is uncommon in families of probands with schizoaffective disorder, schizophrenia, and affective disorder (Angst, Felder, and Lohmeyer 1979a; Mendlewicz, Linkowski, and Wilmotte 1980; Baron et al. 1982). Gershon et al. (1982) found a greater familial risk for schizoaffective disorder with schizoaffective probands compared to probands with affective disorders, but this effect was nonspecific and reflected increased risks for schizophrenia and for affective disorders in families of schizoaffective patients.

In a record study of the morbidity risk for psychosis in over 1,000 first degree relatives of 150 schizoaffective patients, Angst, Felder, and Lohmeyer (1979a) found that the morbidity risk for affective disorder among relatives was somewhat greater than the risk for schizophrenia. Although the authors concluded that "from a genetic viewpoint schizoaffective disorder takes an intermediate position between schizophrenia and affective disorders," no direct comparisons were made with relatives of probands with schizophrenia or affective disorders. Hence, these results are subject to various interpretations. Other researchers have found that the risk for affective disorders is similar in relatives of schizoaffective and affective disorder probands (Tsuang, Dempsey, and Rauscher 1976; Tsuang et al. 1977; Abrams and Taylor 1980; Mendlewicz, Linkowski, and Wilmotte 1980; Baron et al. 1982; Gershon et al. 1982). The morbidity risk for schizophrenia in first degree relatives of schizoaffective patients has been reported to be either as great as the
Since it is generally acknowledged that the terms "schizophrenia" and "affective disorder" designate families of illnesses with a broad range of defining characteristics rather than single, homogeneous diseases, the question of heterogeneity naturally arises in studies of schizoaffective patients. For example, using the same probands and relatives as in their study cited earlier, Angst, Felder, and Lohmeyer (1979b) attempted to answer the question: Are schizoaffective psychoses heterogeneous? They subdivided the probands by sex, age at first episode, number of episodes, schizophrenic subtypes, affective subtypes, and schizoaffective subtypes, but they were unable to detect any significant differences in the morbidity risk among relatives of probands. The only indication of heterogeneity was found when probands were divided according to age of onset: relatives of schizoaffectives were at a higher risk for schizoaffective disorder if the patient became ill between the ages of 20 and 29 years. Although they interpreted their data as confirming the existence of schizoaffective disorder as a third diagnostic entity alongside schizophrenia and affective disorder, their findings did not allow them to distinguish between schizoaffective subgroups using the external criterion of morbidity risk among relatives.

The family and linkage study of Mendlewicz, Linkowski, and Wilmotte (1980), on the other hand, did suggest that schizoaffective disorder is heterogeneous. They concluded that there is a genetic link between schizoaffective disorder and affective disorder on the basis of the high morbidity risk for manic-depressive illness in relatives of schizoaffective patients. However, other factors, such as the unexpectedly high prevalence of schizophrenia in relatives, suggested that some cases of schizoaffective disorder may be traced to genes related to schizophrenia. Procci surveyed the literature in 1976 across a variety of dimensions, including acute symptomatology, response to lithium carbonate therapy, followup studies, family history, and genetics. He concluded that, most likely, schizoaffective psychosis is a heterogeneous entity that includes a number of different pathological states.

Similar results were obtained in a study of 35 psychotic sib pairs conducted by Tsuang (1979). Tsuang compared the actual combinations of psychoses in sib pairs with the combinations that would be expected if schizoaffective disorder were genetically independent, a variant of affective disorder, or a variant of schizophrenia. Results were consistent with the conclusion that affective disorder and schizophrenia, but not schizoaffective disorder, are genetically distinct. Furthermore, these analyses indicated that schizoaffective disorder is genetically heterogeneous, with at least two subtypes: an affective subtype and a schizophrenic subtype. A third, undifferentiated, subtype was also proposed as a means of accounting for patients whose disease resists classification into the schizophrenic or affective subtype, or because of an admixture of strong schizophrenic and affective features, or in cases with insufficient information.

Another approach to analyzing the heterogeneity of schizoaffective disorder is to subtype patients according to the polarity of their affective features. This is the scheme adopted by Spitzer, Endicott, and Robins (1978) in the RDC. Clayton (1982) argued for the usefulness of this approach in a review of studies of schizoaffective manic and schizoaffective depressed patients. Clayton also presented preliminary findings from a small sample of 36 schizoaffective patients indicating that these subgroups can be distinguished on the basis of symptomatology and especially family history. Brockington, Kendell, and Wainwright (1980) and Brockington, Wainwright, and Kendell (1980) reported similar results, and also found distinct differences in the course and outcome, although the depressive subgroup tended to be highly heterogeneous.

The family history comparisons made by Angst, Felder, and Lohmeyer (1979b), on the other hand, provided no evidence for the subtyping of schizoaffective disorder on the basis of polarity or along the lines of the Kraepelinian two-entities tradition.

More recently, Baron et al. (1982) conducted a study of schizoaffective illness, schizophrenia, and affective disorders in first degree relatives of schizoaffective patients who were subdivided according to their symptom patterns into schizophrenic and affective subtypes. The affective subgroup was further subdivided into manic and depressed subtypes using the RDC. Comparisons of the familial patterns of psychotic illness, using matched groups of schizophrenic, unipolar, and bipolar
probands, showed that the schizophrenic subgroup was genetically similar to the schizophrenic group, whereas the affective subgroup resembled the unipolar and bipolar probands. Additional analyses based on small samples suggested that the affective subtype can be meaningfully subdivided into manic and depressive subtypes along the lines of the RDC. In particular, relatives of the schizoaffective-manic subgroup were at greater risk for unipolar and bipolar affective disorders than relatives of the schizoaffective-depressed subgroup, although the differences were not statistically significant. This study clearly demonstrates "the potential utility of diagnostic subtyping in sorting out homogeneous subgroups from among the schizoaffective psychoses" (Baron et al. 1982, p. 259).

Conclusion
Despite the large number of investigations of schizoaffective patients that have been conducted, the principal research problems remain unresolved: the validity of the concept of schizoaffective disorder, and the similarity of schizoaffective patients to patients with typical forms of schizophrenia and major affective disorders. As this survey has indicated, empirical studies can be cited to support several divergent concepts of schizoaffective disorder: that this "disorder" is actually (a) a form of schizophrenia, (b) a form of major affective disorder, or (c) qualifies as a distinct and possibly heterogeneous diagnostic entity.

Evidence can also be cited to support the hypothesis that schizoaffective disorder actually identifies an intermediate region on a unidimensional or hierarchical continuum of psychotic illness. This hypothesis was suggested in part by success in differentially predicting outcome using prognostic scales (Stephens, Astrup, and Mangrum 1966). The blending of schizophrenic and affective symptoms in schizoaffective patients, and the intermediate position (between schizophrenia and major affective disorders) reported by Tsuang and Dempsey (1979) in a study of long-term outcome, are also consistent with the continuum hypothesis. This hypothesis has also been suggested as a means of explaining intransigent problems in the classification of schizoaffective patients when comparisons are made on the basis of history, clinical picture, and outcome (Brockington and Lef 1979; Brockington, Kendell, and Wainwright 1980). In this sense, the concept of a psychotic continuum provides a valuable alternative to diagnostic concepts derived from the Kraepelian two-entities tradition.

The widespread divergence of empirical findings in this area of research does not necessarily indicate that certain studies need to be completely discounted. An alternative and more promising approach is to accept these repeated differences as evidence for the heterogeneity of schizoaffective disorder. Together with differences in selection criteria (arising from different diagnostic concepts) and the inevitable selection factors in hospital studies (Himmelhoch et al. 1981), this heterogeneity could help account for a number of discrepant findings. Faced with evidence of substantial heterogeneity, an appropriate research strategy is to search for homogeneous subgroups of schizoaffective patients (e.g., see Angst, Felder, and Lohmeyer 1979b; Tsuang 1979; Brockington, Kendell, and Wainwright 1980; Brockington, Wainwright, and Kendell 1980; Clayton 1982). This research strategy makes clinical sense as well, because differential diagnosis of schizoaffective patients is needed for treatment choice (e.g., neuroleptics vs. lithium) and prognosis (e.g., chronic course vs. episodic or remitting course).

In order to identify and analyze homogeneous subtypes of schizoaffective disorder, it is helpful to incorporate information about homogeneous subtypes of schizophrenia and major affective disorders. Our current research program—in which schizoaffective patients have been studied using the same procedures for studying the long-term outcome and family data of strictly defined groups of schizophrenics, manics, and depressives—will now be described to illustrate this research strategy.

We have already briefly described the selection of a sample of 85 schizoaffective patients for comparison with 525 patients (the "Iowa 500" sample) meeting the Washington University research criteria (Feighner et al. 1972) for schizophrenia (n = 200), mania (n = 100), and depression (n = 225). The Iowa 500 Study also included a matched group of 160 surgical controls in order to ensure blindness during followup and family interviews, and to provide comparison groups for analyzing outcome and mortality. Additional details are given elsewhere (Tsuang, Dempsey, and Rauscher 1976; Tsuang et al. 1977, 1979).

The schizoaffective sample of 85 patients is a subset of 310 "atypical schizophrenics," who, like the Iowa 500 probands, were hospitalized at the University of Iowa Psychiatric Hospital between 1934 and 1944. Of the 3,800 original admissions during this decade, 510 had received a chart diagnosis of schizophrenia. Of these,
the 310 who did not meet the research criteria of Feighner et al. (1972) were collectively called “atypical” schizophrenics. Using the same blind procedures employed for the Iowa 500 Study, we collected 30- to 40-year followup and family data for these “atypical” schizophrenics, along with a matched control group of 176 surgical patients admitted to the University of Iowa General Hospital during the same period of time (to show the comparison with the earlier study, we have termed this the Iowa Non-500 Study).

We reported above the results of comparing the subgroup of 85 schizoaffective patients with the Iowa 500 Study groups after comparisons were made on the basis of sex, age at admission, precipitating factors, outcome, and a family history of schizophrenia or affective disorder. Briefly, we found that the schizoaffective group differed greatly from the schizophrenics, and most closely resembled the mania group when allowance was made for a younger age at onset and a higher frequency of precipitants (Tsuang, Dempsey, and Rauscher 1976). Comparisons of long-term outcome showed that schizoaffective patients fared better than schizophrenics, but significantly worse than patients with affective disorders (Tsuang and Dempsey 1979).

In our current research, we are continuing the analysis of these 85 schizoaffective patients in order to develop more precise diagnostic criteria for schizoaffective disorder and to determine if subtypes can be identified for purposes of diagnosis and treatment. Additional comparisons are being made with the typical groups of psychotics from the Iowa 500 Study using the variables mentioned above, plus clinical features (rated from admission hospital charts) and family data from blind structured psychiatric interviews with first degree relatives (Tsuang, Woolson, and Simpson 1980). Previous analyses have shown that our groups of schizophrenic and affective disorder patients represent two different nosological conditions (Tsuang, Woolson, and Fleming 1979; Tsuang, Winokur, and Crowe 1980). Furthermore, these groups are relatively homogeneous with respect to lifetime psychiatric diagnoses (Tsuang, et al. 1981) and family data (Tsuang, Winokur, and Crowe 1980).

At present, therefore, we are investigating index admission variables that discriminate between schizophrenia and major affective disorder (according to the final study diagnosis, which incorporates all relevant information including long-term course and family data) to see how well these same variables subclassify schizoaffective patients into “schizophrenic” and “affective” homogeneous subgroups. Other taxonomic procedures are also being used to validate these analyses. Then, by analyzing the characteristics of such subgroups, we are attempting to develop clinical and research diagnostic criteria for the differential diagnosis of schizophrenic patients. The subtyping criteria will be tested and refined by application to the larger study sample of 310 atypical schizophrenics. In the future, we plan to conduct a prospective cohort and family study based on a different population of psychotic patients to test the generality of differential diagnostic criteria developed using our Iowa study samples. We also expect that biological and psychosocial research will eventually play a major role in deciding how to classify and treat patients with schizoaffective features. In closing, it is worth noting that the continuing research interest in the concept of schizoaffective disorder is an indication of the incompleteness and inadequacy of current concepts of schizophrenia and major affective disorders. For this reason, research concerning schizoaffective disorder has the potential to make a major contribution to our understanding and clinical management of the entire spectrum of major psychotic disorders.

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