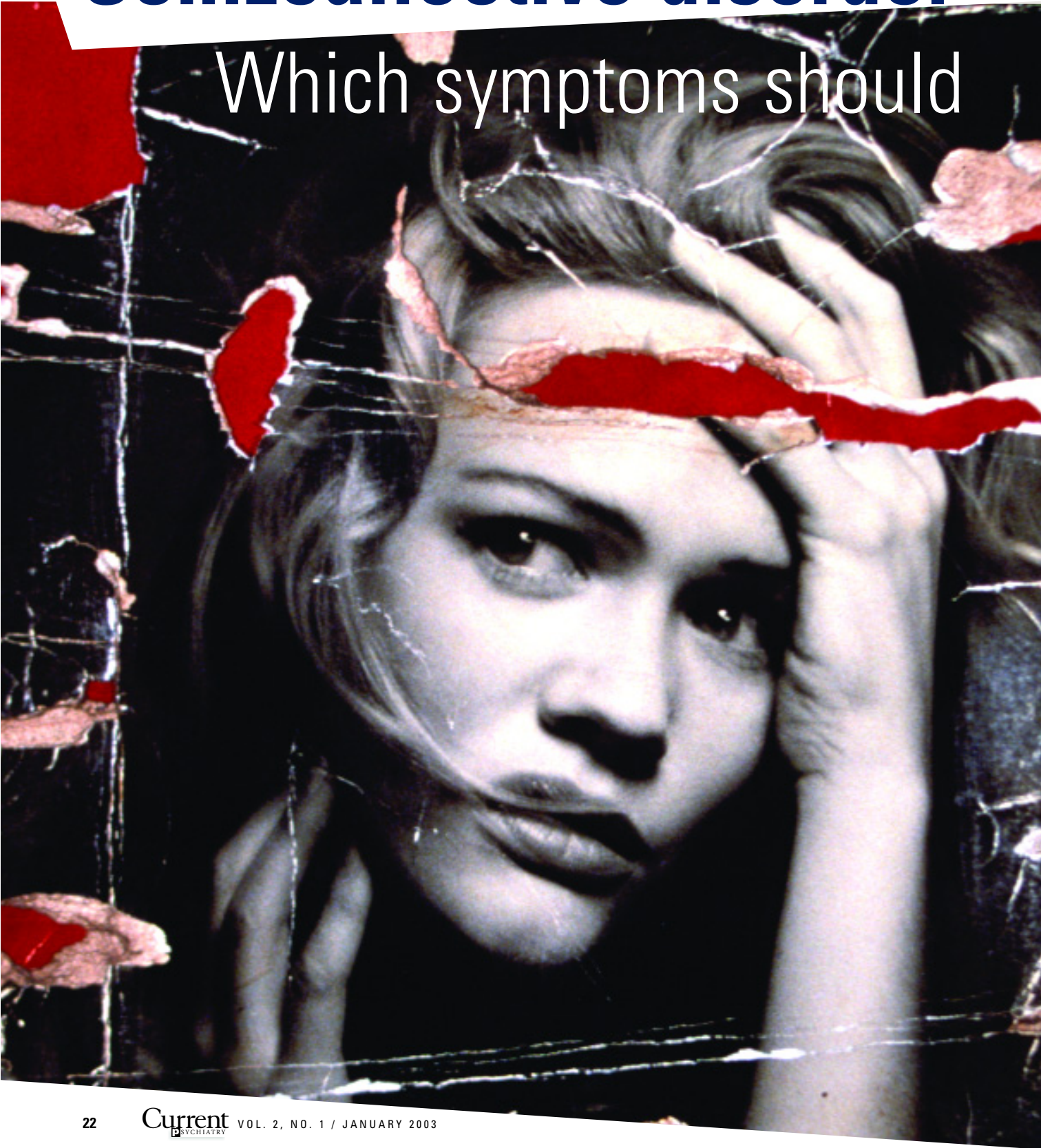


Schizoaffective disorder

Which symptoms should



be treated first?

Stephen M. Strakowski, MD

Professor of psychiatry, psychology, neuroscience, and biomedical engineering
University of Cincinnati College of Medicine
Cincinnati, OH

Patients with schizoaffective disorder present with a complicated mix of psychotic and affective symptoms that confound rational management. All controversy aside, here is a practical approach to treatment.

Psychiatry has used the term “schizoaffective disorder” for more than 60 years, but its specific meaning remains uncertain. Patients who meet its diagnostic criteria typically present with a confusing blend of mood and psychotic symptoms, and we often classify them as being schizoaffective because we don’t know where else to put them.

Much of our difficulty in trying to determine what schizoaffective disorder is can be blamed on insufficient data. We do not know the specific cause of either schizophrenic or mood disorders, and today’s concepts of these broad diagnoses probably encompass multiple etiologies.

Based on the evidence and clinical experience, this article presents:

- the evolution of schizoaffective disorder as a psychiatric diagnosis
- the four main concepts that attempt to explain the disorder’s cause
- and a practical approach for managing these patients’ complicated symptoms.

Origins of schizoaffective disorder

When Jacob Kasanin¹ originated the term schizoaffective disorder in 1933, psychiatry was struggling to integrate Emil Kraepelin’s and Eugene Bleuler’s two competing and complementary schemes for understanding psychotic disorders.

Kraepelin had proposed that the major psychoses could be divided between dementia praecox and manic-depressive insanity (and to a lesser extent, paraphrenia), based on the



Box

DSM-IV CRITERIA FOR SCHIZOAFFECTIVE DISORDER

- A.** An uninterrupted period of illness during which, at some time, there is either a major depressive episode, a manic episode, or a mixed episode concurrent with symptoms that meet Criterion A for schizophrenia:
- Two (or more) of the following**, each present for a significant portion of time during a 1-month period (or less if successfully treated):
1. **delusions**
 2. **hallucinations**
 3. **disorganized speech** (e.g. frequent derailment of incoherence)
 4. **grossly disorganized or catatonic behavior**
 5. **negative symptoms**, i.e., affective flattening, alogia, or avolition
- B.** During the same period of illness, there have been delusions or hallucinations for at least 2 weeks in the absence of prominent mood symptoms.
- C.** Symptoms that meet criteria for a mood episode are present for a substantial portion of the total duration of the active and residual periods of the illness.
- D.** The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Specific type:

Bipolar type: If the disturbance includes a manic or a mixed episode (or a manic or a mixed episode and major depressive episodes)

Depressive type: If the disturbance only includes major depressive episodes.

Source: *Diagnostic and statistical manual of mental disorders (4th ed., TR)*. Washington, DC: American Psychiatric Association, 2000.

presenting symptoms and—importantly—course of illness:²

- Manic-depressive insanity typically included periods of full recovery of mental functions between episodes.
- Dementia praecox was defined by a steady deteriora-

tion of mental function and personality from which patients rarely recovered.

This distinction was a landmark in psychiatry but did not offer a specific understanding of the mental or brain dysfunctions underlying these conditions nor a cross-sectional means to diagnose a patient's condition.

Bleuler was less concerned with predicting course and outcome. Instead, he wished to understand his observations that patients commonly exhibited a disjunction among psychological processes that were integrated in healthy individuals.³ He described the cause of this loss of psychological integration as the “schizophrenias” or, literally, “split mind.” In the schizophrenias, he identified symptoms that seemed to reflect this psychological disjunction, such as flat affect, ambivalence, and splitting of cognition from emotion and behavior.

Because Kraepelin described many of these same symptoms in dementia praecox, clinicians tended to equate the schizophrenias with dementia praecox. However, many more patients with Bleuler's schizophrenia recovered than did those with Kraepelin's dementia praecox (essentially by definition). Therefore, some “schizophrenic” patients appeared to meet Kraepelin's diagnosis of manic-depressive insanity. At this point, Kasanin stepped into the fray with his concept of schizoaffective disorder.

Kasanin's conceptualization

Kasanin recognized that many patients exhibited a blending of Bleuler's schizophrenia symptoms with those of Kraepelin's manic-depressive (affective) illness.¹ Moreover, unlike patients with dementia praecox, these blended patients exhibited:

- good premorbid adjustment
- typically a sudden illness onset with marked emotional turmoil
- few symptoms of withdrawal or passivity
- and a relatively short course with complete recovery.

In reporting these patients and subsequently originating the term “schizoaffective psychosis,” Kasanin tried to identify a homogeneous patient population that could be distinguished from the more broadly conceptualized Bleulerian schizophrenias and the more narrowly defined Kraepelinian categories.

The term “schizoaffective disorder” has evolved from this beginning. Interestingly, most—if not all—of the nine

continued on page 27

continued from page 24

cases reported by Kasanin would be diagnosed with an affective disorder with psychotic features under today's diagnostic criteria.⁴ Nonetheless, the term “schizoaffective disorder” was adopted by psychiatry (particularly in the United States) and has been used to classify patients who present with features of both schizophrenia and affective illness but cannot be clearly described as having either.

Evolutions from DSM-I to DSM-III

In American nosology, schizoaffective disorder was included as a subtype of schizophrenia in DSM-I (1952)⁵ and DSM-II (1968)⁶ and then reclassified in DSM-III (1980)⁷ as a “psychotic disorder not elsewhere classified.” Remarkably, none of these classifications provided criteria for diagnosing schizoaffective disorder.

Shortly before publication of DSM-III, Robert Spitzer, MD, and colleagues at the New York Neuropsychiatric Institute developed diagnostic criteria for schizoaffective disorder as part of their research diagnostic criteria (RDC).⁸ The RDC separated patients with affective and certain types of psychotic symptoms, suggestive of schizophrenia at that time, into two types—schizoaffective mania and schizoaffective depression—based on the polarity of the mood symptoms.

The psychotic symptoms identified as “schizophrenic” by the RDC were certain first-rank symptoms designated by Kurt Schneider, such as delusions of being controlled or mood-incongruent hallucinations. [Note: In recent studies, neither first-rank symptoms nor other subtypes of psychotic symptoms (mood-incongruent delusions or hallucinations) have been shown to specifically identify patients with schizophrenia.^{9,10} In fact, no psychotic symptoms are considered pathognomonic for any specific disorder at this time.]

The RDC also introduced the idea that schizoaffective disorder was distinct from psychotic mood disorder in that:

- psychotic symptoms persisted for a specific period (1 week), during which mood symptoms were absent
- and mood and psychotic symptoms overlapped at some time during the course of illness.

These criteria were then adopted with modifications in DSM-III-R,¹¹ which provided the first widely-accepted, well-defined criteria for schizoaffective disorder.

DSM-III-R and DSM-IV

DSM-III-R defined schizoaffective disorder based on relationships between affective syndromes and the criteria for schizophrenia. Specifically, the diagnosis required the presence of a full depressive or manic syndrome while the patient also met criteria for schizophrenia. To distinguish schizoaffective disorder from psychotic mood disorders, DSM-III-R required that psychotic symptoms persist for 2 weeks in the absence of “prominent” mood symptoms.

Unfortunately, “prominent” was not defined, leaving a fair amount of discretion to clinicians and making it difficult to standardize research studies. In addition, the predictive utility of 2 weeks of psychosis has not been strongly validated. In fact, the time span at which psychosis without a mood disorder identifies a new syndrome is not known.

To rule out schizophrenia, the mood syndrome could not have been “brief” relative to the psychosis; again, what “brief” meant was difficult to put into practice. Notably, there was no specific requirement to rule out mood disorders (i.e., that the psychosis was not brief relative to the duration of mood symptoms).

DSM-IV slightly modified these criteria,¹² but their basic flavor from DSM-III-R was retained. Despite their limitations, the diagnostic criteria in DSM-III-

R and DSM-IV at least provided clinicians and scientists the means to consistently identify schizoaffective disorder. The diagnostic criteria (*Box*) are still considered reliable today.¹³

Few studies exist, so the diagnosis of schizoaffective disorder remains poorly validated

Four concepts of schizoaffective disorder

Relatively few studies of schizoaffective disorder exist, so the diagnosis remains poorly validated. At least four concepts have been developed (*Figure*).⁴

Concept 1: Schizoaffective disorder is a variant of schizophrenia. Many of the characteristics of schizoaffective disorder that Kasanin first described, such as rapid onset and confusion, were identified as good prognostic indicators in later concepts of schizophrenia. Some family history studies also suggest a link between schizophrenic and schizoaffective disorders.¹⁵

Concept 2: Schizoaffective disorder is a variant of mood disorder.⁹ Schizoaffective disorder represents a pernicious type of mood disorder in which psychotic symptoms persist and the



Figure

FOUR CONCEPTS THAT SEEK TO EXPLAIN SCHIZOAFFECTIVE DISORDER

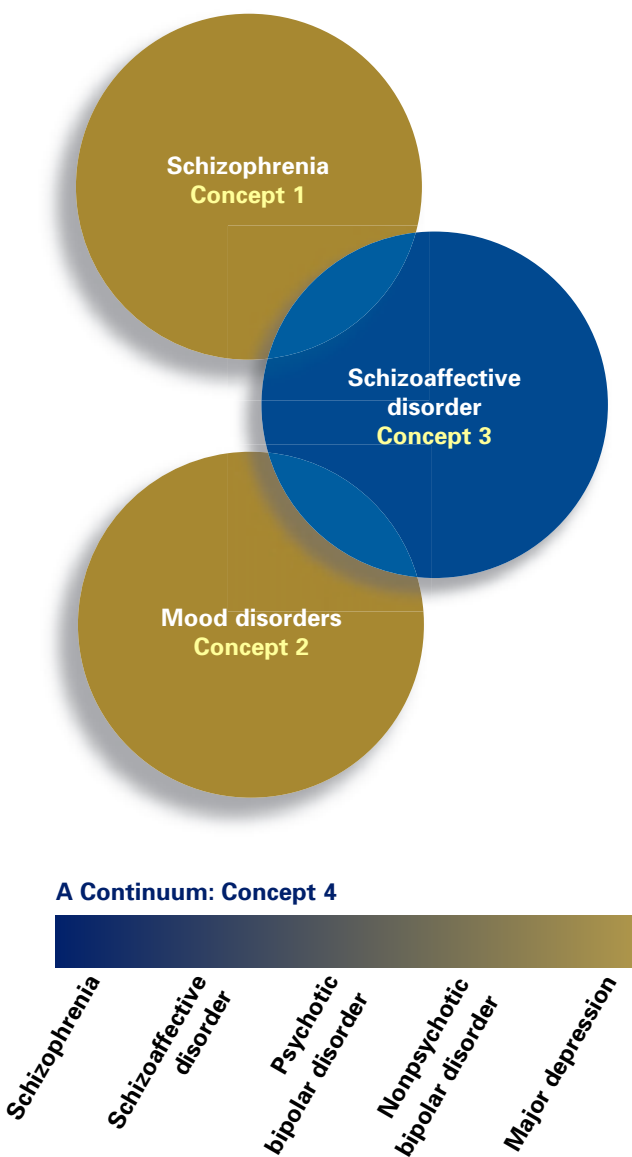


Figure. Four conceptualizations explain schizoaffective disorder as (1) a type of schizophrenia; (2) a type of mood disorder; (3) a heterogeneous combination of patients with schizophrenia, mood disorder, and “real” schizoaffective disorder; and (4) as part of a continuum of psychotic disorders from worst prognosis (schizophrenia) to best prognosis (major depression).

course of illness is worse than in other variants (although better than in schizophrenia).¹⁶ Family studies are unclear about links between mood and schizoaffective disorders.¹⁷

Concept 3: Schizoaffective disorder represents a heterogeneous combination of schizophrenia and mood disorder. Specifically, schizoaffective disorder may comprise a group of patients with severe psychotic mood disorders and either good-prognosis schizophrenia or schizophrenia with numerous affective symptoms.

A subgroup of patients with “true” schizoaffective disorder (distinct from schizophrenic or mood disorders) might also exist.¹⁸ As a twist on this idea, others have suggested that schizoaffective disorder, bipolar type is simply a variant of bipolar disorder, whereas schizoaffective disorder, depressed type is more closely akin to schizophrenia. The fact that depression occurs at some time in most patients with schizophrenia supports this view.

Concept 4: Psychotic disorders share a genetic vulnerability and exist on a continuum (from worst to best prognosis) from schizophrenia, to schizoaffective disorder, to psychotic then nonpsychotic bipolar and major depressive disorders.¹⁹

A lack of definitive evidence prevents us from choosing among these concepts; good studies support and discount each possibility.

Patient management

When faced with a patient who meets criteria for schizoaffective disorder, I believe practical considerations can guide treatment. The label “schizoaffective disorder” reminds us to consider treatment of these patients broadly (in contrast, for example, to the label “schizophreniform disorder,” which implies a stronger link to schizophrenia than outcome studies support²¹).

Treat the mood component first. In most patients with schizoaffective disorder, it is difficult to distinguish between diagnoses of schizophrenia or mood disorder. It is prudent to begin by aggressively treating the mood component, because psychotic mood disorders generally respond more favorably to treatment than does schizophrenia. Use mood stabilizers for patients with a history of mania and antidepressants in depressed patients with no history of mania.

As is true for psychotic mood disorders, concurrent administration of an antipsychotic is often warranted. Recent studies strongly suggest that atypical antipsychotics are preferred over traditional neuroleptics to treat psychotic patients

Related resources

- ▶ National Mental Health Association factsheet on schizoaffective disorder www.nmha.org/infoctr/factsheets/52.cfm
- ▶ Reichenberg A, Weiser M, Rabinowitz, J, et al. A population-based cohort study of premorbid intellectual, language, and behavioral functioning in patients with schizophrenia, schizoaffective disorder, and nonpsychotic bipolar disorder. *Am J Psychiatry* 2002;159(12):2027-35.
- ▶ Robinson DG, Woerner, MG, Alvir JM, et al. Predictors of medication discontinuation by patients with first-episode schizophrenia and schizoaffective disorder. *Schizophr Res* 2002;57(2-3):209-19.

in general, and this preference extends to patients with schizoaffective disorder.^{4,14,20}

Some—if not most—atypical antipsychotics may have mood-stabilizing or antidepressant properties and may permit monotherapy of patients with schizoaffective disorder. Controlled clinical trials have not examined these agents as long-term maintenance therapy for the mood component of schizoaffective disorder, however. Until such studies are completed, many patients may require long-term mood-stabilizer or antidepressant therapy, with or without ongoing antipsychotic treatment.^{4,14}

The next step. Alternate treatments should be considered for patients in whom trials of atypical antipsychotics have failed, both in combination with thymoleptics and in monotherapy. Conventional antipsychotics, particularly depot formulations, are a reasonable intervention, particularly in schizoaffective patients with minimal mood symptoms.

Clozapine remains a first-line choice for patients with treatment-resistant psychotic disorders and should be considered in patients with treatment-resistant schizoaffective disorder as well.

Conclusion

Patients meeting criteria for schizoaffective disorder typically present with a complex and confusing combination of affective and psychotic symptoms. The diagnosis continues to be applied predominantly to patients who are otherwise difficult to classify, and the diagnostic criteria supporting the presence of a distinct condition remain poorly validated.

Schizoaffective disorder probably defines a heterogeneous group of patients, but—practically speaking—they can often be managed by following algorithms for psychotic mood disorders.^{4,13} The most prudent long-term approach seems to be to keep treatment options flexible, with careful

attention to managing symptoms as they wax and wane, rather than rigidly fixing on a single medication or type of medication.

References

1. Kasanin J. The acute schizoaffective psychoses. *Am J Psychiatry* 1933;113:97-126.
2. Kraepelin E. Dementia praecox and paraphrenia, together with manic depressive insanity. Translated from original texts by The Classics of Psychiatry and Behavioral Sciences Library. Delran, NJ; Gryphon Editions, 1993.
3. Bleuler E. Text-book of psychiatry. Translated from original texts by The Classics of Psychiatry and Behavioral Sciences Library. Delran, NJ: Gryphon Editions, 1994.
4. Keck PE, Jr, McElroy SL, Strakowski SM, West SA. Pharmacologic treatment of schizoaffective disorder. *Psychopharmacology* 1994;114:529-38.
5. *Diagnostic and statistical manual of mental disorders*. Washington, DC: American Psychiatric Association, 1952.
6. *Diagnostic and statistical manual of mental disorders (2nd ed)*. Washington, DC: American Psychiatric Association, 1968.
7. *Diagnostic and statistical manual of mental disorders (3rd ed)*. Washington, DC: American Psychiatric Association, 1980.
8. Spitzer RL, Endicott J, Robins E. Research diagnostic criteria. Rationale and reliability. *Arch Gen Psychiatry* 1978;35:773-82.
9. Pope HG, Jr, Lipinski JF. Diagnosis of schizophrenia and manic-depressive illness: a reassessment of the specificity of 'schizophrenic' symptoms in the light of current research. *Arch Gen Psychiatry* 1978;35:811-28.
10. Strakowski SM, McElroy SL, Keck, Jr, PE, West SA. Racial influence on diagnosis in psychotic mania. *J Affect Disord* 1996;39:157-62.
11. *Diagnostic and statistical manual of mental disorders (3rd ed, rev)*. Washington, DC: American Psychiatric Press, 1987.
12. *Diagnostic and statistical manual of mental disorders (4th ed)*. Washington, DC: American Psychiatric Press, 1994.
13. Keck PE, Jr, McElroy SL, Strakowski SM. New developments in the pharmacologic treatment of schizoaffective disorder. *J Clin Psychiatry* 1996;57S:41-8.
14. Clayton PJ. Schizoaffective disorders. *J Nerv Ment Dis* 1982;170:646-50.
15. Kendler KS, Spitzer RL, Williams JBW. Psychotic disorders in DSM-III-R. *Am J Psychiatry* 1989;146:953-62.
16. Strakowski SM, Keck PE, Jr, Sax KW, McElroy SL, Hawkins JM. Twelve-month outcome of patients with DSM-III-R schizoaffective disorder: comparisons to matched patients with bipolar disorder. *Schizophrenia Res* 1999;35:167-74.
17. Maier W, Lichtermann D, Minges J, Heun R, Hallmayer J, Benkert O. Schizoaffective disorder and affective disorders with mood-incongruent psychotic features: keep separate or combine? Evidence from a family study. *Am J Psychiatry* 1992;149:1666-73.
18. Kendler KS, McGuire M, Gruenberg AM, Walsh D. Examining the validity of DSM-III-R schizoaffective disorder and its putative subtypes in the Roscommon Family Study. *Am J Psychiatry* 1995;152:755-64.
19. Crow TJ. A continuum of psychosis, one human gene and not much else—the case for homogeneity. *Schizophrenia Res* 1995;17:135-45.
20. Strakowski SM, DelBello MP, Adler CM. Comparative tolerability of drug treatments for bipolar disorder. *CNS Drugs* 2001;15:701-18.
21. Strakowski SM. Diagnostic validity of schizophreniform disorder. *Am J Psychiatry* 1994;151:815-24.

Patients diagnosed with schizoaffective disorder present with a complex mixture of psychotic and affective symptoms. Practically speaking, such patients can often be managed by following treatment algorithms for psychotic mood disorders.

BottomLine