

## SCHIZOAFFECTIVE DISORDER

Schizoaffective disorder was first described in the literature by Kasanin in 1933, referring to a group of patients in whom both psychotic ("schizo") and mood ("affective") symptoms are prominent features. A formal diagnosis of schizoaffective disorder requires that (1) a mood episode (major depressive, manic, or mixed) co-occurs with active schizophrenia symptoms; (2) hallucinations or delusions have occurred for at least 2 weeks in the absence of prominent mood symptoms; (3) the mood symptoms are present for a substantial portion of the total active and residual phases of schizophrenia; and (4) the symptoms are not related to the direct physiological effects of a substance or a general medical condition. Schizoaffective disorder can be further broken down into two subtypes: depressive type (if the mood component consists of only major depressive episodes) and bipolar type (if a manic or mixed episode is part of the mood component). Because loss of interest or pleasure also resembles another common symptom of schizophrenia (i.e., anhedonia), the other essential feature of a major depressive episode, pervasive depressive mood, must be present in the depressive type of schizoaffective disorder.

### Differentiation from Schizophrenia and Mood Disorder

Schizoaffective disorder is distinguished from schizophrenia and from mood disorder with psychotic features in modern diagnostic systems such as the DSM-IV and ICD-10. For example, psychotic symptoms occurring exclusively during mood disturbances are counted toward a diagnosis of mood disorder with psychotic features. In schizoaffective disorder, mood symptoms must overlap with active psychotic symptoms for 2 weeks or more and must be present for a substantial portion of the total duration of illness. Therefore, mood episodes that have never co-occurred with active schizophrenia symptoms or are brief relative to the entire history of schizophrenia are considered mood disorder superimposed on schizophrenia. Although the DSM-IV-TR (American Psychiatric Association, 2000) provides specific descriptions for making differential diagnosis, it has proven to be a difficult task. One of the reasons is its reliance on a very detailed history taking, which is rarely accomplished in clinical settings because of time constraints and the limited amount and reliability of information. Additionally, because the relative proportion of mood to psychotic symptoms may change as the illness evolves (e.g., new mood or psychotic episodes emerge), a diagnosis of schizoaffective disorder may be appropriate at one time but not at another.

The effort to establish differential diagnosis is based on the assumption that schizoaffective disorder is a disease entity distinct from schizophrenia and mood disorder. However, mood symptoms are very common in schizophrenia, and psychotic symptoms can occur in mood

disorders. Research comparing these three diagnostic categories for demographic characteristics, symptom manifestation, clinical course, response to treatment, neuroimaging data, family morbidity, and genetic findings generally indicates that schizoaffective disorder lies between schizophrenia and mood disorder without clear-cut boundaries (Cheniaux et al., 2008). It remains under debate as to whether schizoaffective disorder represents comorbid schizophrenia and mood disorder or is instead a midpoint on a continuum between schizophrenia and mood disorder.

### Epidemiology

Few epidemiological studies have been conducted on schizoaffective disorder. As would be expected from the disorder's poor diagnostic stability and the use of varying diagnostic criteria in different studies, little has been established regarding its incidence, prevalence, demographic factors, and whatever risk factors may be associated with it. The average lifetime prevalence rate has been estimated to be 0.5% in the general population (Mahli, Green, Fagiolini, Peselow, & Kumari, 2008). The disorder appears to affect more women than men. As in schizophrenia, the typical age of onset has been reported to be late adolescence or early adulthood.

### Etiology

It remains unclear what causes schizoaffective disorder. However, results from family studies and twin studies present strong evidence for genetic factors in the disorder. For example, lifetime prevalence of major affective disorders has been found to be three to five times higher in relatives of individuals with affective disorder than in normal controls (Gershon et al., 1982). Schizoaffective disorder also seems to share genetic susceptibility with schizophrenia and affective disorders. Higher rates of psychotic mood disorders have been reported in first-degree relatives of schizophrenic probands, and vice versa. A twin study showed higher correlations between schizophrenia, schizoaffective disorder, and manic syndrome among monozygotic twin pairs than among dizygotic twins (Cardno, Rijdsdijk, Sham, Murray, & McGuffin, 2002). Although no genes have been uniquely linked to schizoaffective disorder, genetic studies have found several overlapping genes between affective disorders and schizophrenia. Chromosomal regions such as 13q and 22q are the most robustly replicated regions. Proponents of the notion of a continuum between schizophrenia and mood disorder speculate that these shared genes also play an etiological role in schizoaffective disorder.

There are several theoretical models for how the same genetic susceptibility may result in different disorders along the schizophrenia-affective disorder spectrum. For example, the quantitative multiple threshold model

postulates that the risk imposed by these overlapping genes is cumulative; schizoaffective disorder is the consequence of the presence of genetic predisposition higher than the threshold for bipolar disorder but lower than that for schizophrenia. The gene-gene interaction model suggests that the same genes for schizophrenia and bipolar disorder with different genetic combinations may result in the development of schizoaffective disorder. The allelic heterogeneity model describes a distinctive mutation within the same genes that might demarcate schizoaffective disorder from other disorders (Kelsoe, 2007). Recent data suggest that genetic liability (e.g., variation or mutation in 22q11) may lead to the development of schizophrenia and schizoaffective disorder through the process of structural (e.g., decreased density of gray and white brain matter) and functional (e.g., dysregulation of neurotransmitters such as dopamine and serotonin) disturbances of the brain.

However, genetic factors cannot provide a full etiological account for schizoaffective disorder, because the chance for an identical twin of a person diagnosed with schizoaffective disorder to develop the disorder is far less than 100%. It follows that environmental factors also contribute significantly to the development of schizoaffective disorder. The diathesis-stress model, in which the development and relapse of the disorder is conceptualized as a result of an interaction between genetic predisposition and psychosocial stressors (e.g., loss of job, high expressed emotion within family), is a widely accepted etiological model of schizophrenia-spectrum disorders.

### Prognosis

Although schizoaffective disorder very often resembles schizophrenia in terms of symptoms, its clinical course appears to be more similar to that of bipolar disorder (Benabarre et al., 2001). Bipolar schizoaffective patients tend to have a greater number of episodes and more episodes per year with shorter episodes and cycles than unipolar schizoaffective (i.e., depressive-schizophrenic) patients. The outcome of schizoaffective disorder is generally better than that of schizophrenia but worse than that of psychotic affective disorders. Poor prognostic outcome is more likely to occur in patients with poor interepisode recoveries, persistent psychotic symptoms without affective features, poor premorbid social adjustment, psychotic features with incongruent mood, chronicity of the illness, and persistent negative schizophrenia symptoms (Reinares, Vieta, Benabarre, & Marneros, 2007). Good prognostic factors include high premorbid functioning, existence of precipitating factors, and a family history of affective disorder.

### Treatment

Pharmacological treatment of schizoaffective disorder often combines medications targeting psychotic symptoms

with those targeting affective symptoms. Commonly prescribed classes of medication to treat acute symptoms and for maintenance purposes include antipsychotics (e.g., olanzapine, clozapine, risperidone), antidepressants (e.g., citalopram, fluoxetine, sertraline, venlafaxine), mood stabilizers (e.g., carbamazepine, lithium, valproate), and benzodiazepines (e.g., alprazolam, clonazepam, lorazepam). As in other psychiatric illnesses, treatment response to a particular medication (or combination of medications) varies widely from one patient to another. About 30% of patients with schizoaffective disorder do not respond or respond partially to pharmacological treatment. Management of these treatment-resistant cases includes increasing the medication dose, switching to another medication with a different psychopharmacological profile, and adding another psychotropic medication. Electroconvulsive therapy (ECT) may be used in refractory cases showing limited response to medications.

Whereas pharmacotherapy is the first-line treatment of schizoaffective disorder, psychosocial interventions may be employed as an adjunct to medications to better address aspects such as social functioning and quality of life. Cognitive behavioral therapy (CBT), interpersonal therapy (IPT), and family therapies are commonly conducted psychosocial interventions for patients with schizoaffective disorder. Research data on the efficacy of psychotherapies for schizoaffective disorder are scarce; most randomized controlled clinical trials have focused on schizophrenia, depression, and bipolar disorder. A recent review of outcome research on CBT for severe and chronic schizophrenia and mood disorders suggests that CBT is effective for the reduction of positive and negative symptoms in schizophrenia and of depressive features in depression, as well as for the prevention of relapse in bipolar disorders (Scott, 2007). Preliminary findings suggest that CBT can also be beneficial for schizoaffective disorder. More research is needed to confirm the efficacy of CBT and other psychotherapies for schizoaffective disorder.

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#### SUGGESTED READINGS

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See also: Mood Disorders; Schizophrenia