Schizoaffective Disorder

Andreas Marneros

Department of Psychiatry, Psychotherapy and Psychosomatics, Martin Luther University, Halle-Wittenberg, Germany

Schizoaffective disorders are a controversially discussed but existing nosological category describing an episodic condition meeting the criteria of both schizophrenia and mood disorders and lying on a continuum between these two prototypes. Both DSM-IV and ICD-10 classify them within the group of "schizophrenia, schizotypal and delusional disorders" with ICD-10 not requiring the absence of mood symptoms for a certain time. Cross-sectionally, schizoaffective disorder can be subdivided into schizodepressive, schizomanic and mixed types. In a longitudinal way, unipolar and bipolar types are distinguished. The division into schizo-dominated and mood dominated types is based on the severity and dominance of the schizophreniform symptomatology and implies significant consequences for treatment and prognosis. In addition, concurrent types should be differentiated from sequential types. Schizoaffective disorder is not rare; lifetime prevalence is estimated at 0.3%. About one third of all psychotic patients suffer from schizoaffective disorder. About two thirds of the patients do not only have schizoaffective episodes but also pure schizophreniform or mood episodes or episodes of acute and transient psychotic disorder. In more than 50% of the patients, symptoms remit more or less completely. The others suffer from light, moderate or severe residual states, which might affect their social adaptation. The suicide rate in schizoaffective disorder is about 12%. The treatment of schizoaffective disorder primarily is a combination of antipsychotics and mood stabilizers or antidepressants. Long-term prophylactic treatment mainly consists of antipsychotics and mood stabilizers. Differential diagnosis of schizoaffective disorder is not at all easy. It must be distinguished from psychotic mood disorder, where the psychotic symptoms are mood-congruent. Although DSM-IV allows even mood-incongruent psychotic symptoms in psychotic mood disorder, these cases should better be allocated to schizoaffective disorder. Schizoaffective disorder must also be distinguished from schizophrenia with mood symptoms. In the latter, the mood symptoms are not complete and not so prominent to meet the criteria of a mood episode, or they occur after the schizophreniform have remitted. Sometimes, schizoaffective disorder is mixed up with acute and transient psychotic disorder, although these two conditions do not have very much in common. (Korean J Schizophr Res 2012;15:5-12)

Key Words : Schizoaffective disorder · Definition · Diagnosis.

What is Schizoaffective Disorder?

The term schizoaffective disorder describes a symptomatological constellation meeting the criteria of mood episodes (depressive, manic or mixed) as well as those of schizophreniform episodes.

Not every depressive or maniform symptom, though, can turn a schizophreniform episode into a schizoaffective one. Instead, the complete symptomatology of a depressive, manic or mixed mood episode must be present. This limitation is essential for two reasons : 1) Isolated mood symptoms, especially depressive ones, are common in schizophrenia. They, however, do not qualify a schizophreniform episode or a schizophrenic course as schizoaffective ; and 2) The tendency to overdiagnose schizoaffective disorder in order to avoid potential stigmatization by the diagnosis of schizophrenia can be stopped. Yet, a new trend became apparent in recent times : overdiagnosis of psychotic mood disorder instead of schizoaffective disorder, which may have unforeseeable consequences.

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Address for correspondence: Andreas Marneros, Klinik und Poliklinik für Psychiatrie, Psychotherapie und Psychosomatik Martin-Luther-Universität Halle-Wittenberg 06097 Halle Germany
Tel: 49-345-557 3651
E-mail: andreas.marneros@medizin.uni-halle.de

Schizoaffective disorder in ICD-10, DSM-IV and DSM-5 proposal

ICD-10[1] uses the following diagnostic criteria for schizoaffective disorder :

G1. The disorder meets the criteria of one of the affective disorders (F30, F31, F32) of moderate or severe degree, as specified for each category.

G2. Symptoms from at least one of the groups listed below

must be clearly present for most of the time during a period of at least 2 weeks :

1) Thought echo, thought insertion or withdrawal, thought broadcasting.

2) Delusions of control, influence or passivity, clearly referred to body or limb movements or specific thoughts, actions or sensations ;

3) Hallucinatory voices giving a running commentary on the patient's behaviour or discussing the patient between themselves, or other types of hallucinatory voices coming from some part of the body ;

4) Persistent delusions of other kinds that are culturally inappropriate and completely impossible, but not merely grandiose or persecutory, e. g. has visited other worlds ; can control the clouds by breathing in and out ; can communicate with plants or animals without speaking ;

5) Grossly irrelevant or incoherent speech, or frequent use of neologisms ;

6) Intermittent but frequent appearance of some forms of catatonic behaviour, such as posturing, waxy flexibility and negativism ;

G3. Criteria G1 and G2 above must be met within the same episode of the disorder, and concurrently for at least part of the episode. Symptoms from both G1 and G2 must be prominent in the clinical picture.

G4. Most commonly used exclusion clause. The disorder is not attributable to organic mental disorder or to psychoactive substance-related intoxication, dependence or withdrawal.

Diagnostic criteria for schizoaffective disorder in DSM-IV[2] slightly differ from those in ICD-10, as shown in the following :

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.

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.

For DSM-5, only moderate changes have been proposed in order to make diagnoses more reliable. It is, however, pointed out that for a final definition of schizoaffective disorder much more data from longitudinal studies is required. The proposed changes concern criteria B and C. The DSM-IV term "prominent mood symptoms" is vague, and therefore the term "symptoms meeting criteria for a major mood episode" is recommended. For criterion C, the term "a substantial portion" is recommended to be replaced by the term "over 30%" and the term "total duration" by "life time". The changes "will likely improve the reliability of diagnosis, possibly decreasing the frequency with which it will be made".[3]

What are similarities and differences in the definitions of both classification systems?

After long discussions, both systems decided to classify schizoaffective disorder within the group of "schizophrenia, schizotypal and delusional disorders", which illustrates that schizophrenia and schizoaffective disorder are not identical but somehow belong together. Attempts to classify schizoaffective disorder as a distinct entity or to include them in the group of mood disorders failed due to the data available being rather unclear and inhomogeneous.

The most prominent difference between the two systems is that ICD-10 does not require the absence of mood symptoms for a certain time, which makes diagnoses a little more realistic than those according to DSM-IV and probably of DSM-5.

What are the deficits of ICD and DSM in regard to the definition of schizoaffective disorder?

The simple fact that both systems now define and criteriologically delineate schizoaffective disorder and determine various subtypes must be regarded as a clear progress, considering the long controversies about its existence and characteristics. It is rather unessential whether schizoaffective disorder is included in a schizophrenia category or in a mood disorder category ; there are pros and cons for both allocations. Although both systems comprise a bipolar and a depressive type, there is a substantial difference between ICD-10 and DSM-IV : DSM accounts for the longitudinal course and thus defines two subtypes : a bipolar and a depressive one similar to the differentiation of mood disorders, whereas ICD defines manic, depressive and mixed subtypes, depending on the current episode but not on the longitudinal course, which must be considered a deficit not only for research but also in terms of treatment strategies.

Yet, the most important problem with both systems con-

cerns the definition of schizoaffective disorder *per se.* While the main problem with ICD-10 concerns the longitudinal aspect, the issue with DSM-IV is related to the cross-sectional as well as to the longitudinal definition. It is the chronological criterion B of the DSM-IV definition - the 2 weeks' absence of mood symptoms - that causes problems. The intention of DSM-IV (and DSM-5) was a higher reliability of diagnosis as well as a differentiation between "schizoaffective disorder", "psychotic depression" and "psychotic mania", after even "schizophrenic first-rank symptoms" have been accepted as symptoms of psychotic depression or mania by DSM-IV (and presumably also by DSM-5). This chronological criterion, however, is rather arbitrary and causes an imbalance in favour of the schizophrenic part with the corresponding prognostic shift.

Both systems do not answer the question of what disorder patients have who show alternating schizophrenic, schizoaffective and mood episodes in the course of their disorder. This phenomenon can be seen quite frequently during long-term course.[4,5] Comparative studies of such sequential types and concurrent types - those combining schizophreniform/schizophrenic and mood symptoms in one episode - reveal many similarities at all levels and only a few differences regarding sociodemographic variables and course and prognosis.[6] Hence, criticism of the fact that both systems only offer cross-sectional diagnoses without considering the longitudinal aspect is justified (DSM-IV defines the longitudinal polarity of mood, but does not consider the presence of pure mood or schizophrenic episodes, which becomes apparent when trying to diagnose schizophrenic or mood disorders during course with one of the two systems. The following example (Fig. 1) may illustrate this problem :

In a group of 277 patients which had been diagnosed with bipolar disorder on the basis of their index episode, only 8% could longitudinally be allocated to schizoaffective bipolar disorder and 36% to bipolar mood disorder after a long-term course of 17 years, whereas the majority (56%) could not be allocated to one or the other category, because they also had schizophrenic, schizoaffective and/or mood episodes during the course of their disorder. To solve this problem, the longitudinal axes and the so-called sequential types should be considered in future. Much more intense research is, however, needed to increase reliability.[6,7]

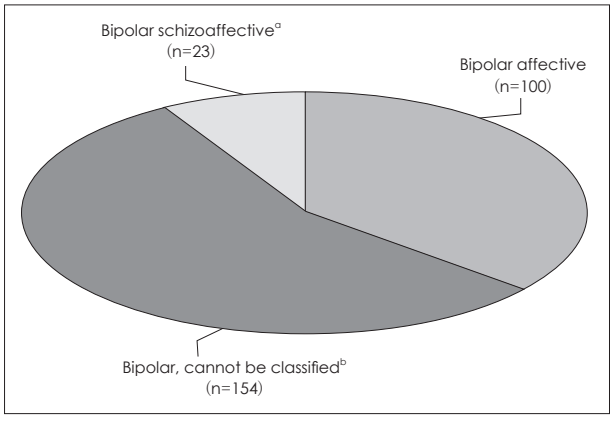

Fig. 1. Bipolar patients (n=277) allocation according to ICD-10. [a] : Only schizoaffective episodes, [b] : Due to schizophrenic, affective and/or schizoaffective episodes occurring at the same time.

Hence, it can be concluded that, due to the unsystematic data available, both classification systems cannot answer the question of which disorder people with alternating schizophreniform, mood and schizoaffective episodes suffer from. There is, however, growing evidence, especially from research on the course of schizophrenic and mood disorders, that they belong to the group of schizoaffective disorder.

Subtypes of Schizoaffective Disorder

Depending on the mood constellation of the disorder, several cross-sectional and longitudinal types can be described.

Based on the cross-sectional symptomatology of the episode, schizoaffective disorders can, according to ICD-10, be subdivided into

- Schizodepressive type (or schizoaffective disorder, depressive type)
- Schizomanic type (or schizoaffective disorder, manic type)
- Mixed schizoaffective type (or schizoaffective disorder, mixed type)

Please note : episodes are always characterized by their mood component.

In *schizodepressive* episodes, criteria of a depressive episode exist in addition to the schizophreniform symptom constellation. *Schizomanic* episodes are characterized by additional manic episodes. And in a mixed schizoaffective episode, the criteria of a *mixed* mood episode as described in ICD-10, DSM-IV and probably also in DSM-5 are met in addition to schizophreniform symptoms. The most frequent type of episodes within schizoaffective disorder is the schizodepressive type, whereas mixed schizoaffective episodes are rather infrequent, even if these are mostly underdiagnosed. The most important reason for underdiagnosing schizoaffective mixed episodes is the conglomeration of symptoms from different areas (schizophreniform, manic and depressive), which can be more or less intense or marked. The most impressing ele-

ment - either manic or depressive - influences the diagnosis and the mixture of symptoms tends to remain unconsidered. Systematic studies, however, have shown that the frequency of schizoaffective mixed episodes is similar to that of mixed episodes in the course of pure mood disorders.[8] According to our own investigations, one third of patients with schizoaffective disorder have at least one mixed episode during the course of their disorder, which seems to be more unfavourable than other types in terms of therapy and prognosis.[9]

Another way to categorize schizoaffective episodes according to their mood component - especially in a longitudinal way - is the distinction of bipolar and depressive (monopolar or unipolar) types, as has been mentioned before. The bipolar type is characterized by the presence of manic and/or mixed symptoms in addition to the depressive symptoms, whereas the depressive type is characterized by the presence of depressive symptomatology throughout the course.

Unipolar and bipolar schizoaffective disorders show significant differences, similar to those between unipolar and bipolar mood disorders.[10-12] The most important of these differences are :

- Gender distribution (more females with unipolar types)
- Premorbid personality (sthenic self-confident personality more frequent in bipolar types)
- Age at first manifestation (younger in bipolar types)
- Frequency of episodes and cycles (more in bipolar types)
- Cycle length (shorter in bipolar types)
- Interval length (shorter in bipolar types)
- Prophylactic response to mood stabilizers (better in bipolar types)

Yet, clinic reality shows that further differentiation is needed. A *schizo-dominated* type must be distinguished from a *mood-dominated* type - on the basis of the severity and dominance of the particular symptom complex. This implies significant consequences for therapy and prognosis. Schizo-dominated types resemble schizophrenia, including their prognosis being less favourable than that of mood-dominated types, which resemble mood disorders and show a similar response to prophylactic treatment.

In addition, *concurrent* types should be differentiated from *sequential* types. As mentioned above, these types do not differ significantly with regard to the premorbid and prognostic levels.[13]

A Short (Hi)story of a Long Controversy

The term "schizoaffective" goes back to the American psychiatrist Kasanin who, in 1933, described nine cases that could neither be allocated to schizophrenia nor to mood disorder. From Kasanin's concept, however, only the term "schizoaffective" survived, as his cases can be better described as "acute and transient psychotic disorder" according to modern criteria.[5,14] What we call "schizoaffective" today, bears much more resemblance to Kurt Schneider's "cases in-between".[15] Schneider exactly described the psychopathological picture of schizoaffective psychoses but named them "schizophrenia", following Karl Jasper's principle of schizophrenic symptoms relativizing the diagnostic valence of mood symptoms. The original concept of schizoaffective disorder can probably be ascribed to Karl Kahlbaum.[16] Emil Kraepelin also knew such states. He described them as numerous and a challenge to or even a weakness of his dichotomy concept.[17] Both Eugen and Manfred Bleuler knew schizoaffective psychoses ; they named them "mixed psychoses" and allocated them to schizophrenia.[18,19] Jules Angst was the first to consequently examine schizoaffective psychoses. In his pioneering book of 1966,[20] not only the bipolar disorders were re-born, but he also investigated schizoaffective psychoses. In contrast to his teacher Manfred Bleuler, he allocated them to mood disorders. After a long definitional and conceptual odyssey, schizoaffective disorders were introduced into the official nomenclature in DSM-I,[21] whereas ICD first used the term in its 9th edition.[22] In the last years, there was a turn towards reason and clinical reality in the ongoing discussion about existence and characteristics of schizoaffective disorders:[23,24] the intermediate position of schizoaffective disorder - between schizophrenia and mood disorders - that has been favoured by various researchers over decades - is currently being confirmed by genetic research.[25-27]

In summary, the current opinion is that schizoaffective disorders form a heterogeneous group of disorders ; they cannot be completely allocated to schizophrenia or mood disorders but lie on a continuum between both prototypes and are the psychopathological expression of a probably genetically determined overlap of affective and schizophrenic spectra.[28-32]

Epidemiology

Only in the last few years, systematic epidemiological studies were conducted on the prevalence of schizoaffective disorder, mostly in clinic populations. In a big national Finnish general population survey, Perälä *et al*.[33] found a lifetime prevalence for all psychotic disorders of 3.06%. Prevalence for schizoaffective disorder was estimated to be 0.32%, com-

pared to 0.87% for schizophrenia, 0.24% for bipolar I disorder, 0.35% for depressive disorder with psychotic symptoms and 0.18% for persistent delusional disorder. This study evidences what has also been found by clinical studies, namely that schizoaffective disorder is not at all rare. Twenty to thirty percent of all so-called endogenous psychoses (which means schizophrenia and mood disorder) are schizoaffective disorders. An international study considering several countries on several continents found schizoaffective disorder in more than 31% of all psychotic patients.[34)]

Course

Prognosis : Schizoaffective disorder mostly (60%) has a polyphasic course, which means it consists of more than three episodes. Oligophasic course (less than three episodes) is rare (20%), and monophasic course hardly ever occurs (10%)(Fig. 2).[4)]

The frequency of episodes depends on how successful the prophylactic therapy is and on whether it is a bipolar or unipolar disorder. Bipolar disorders, as mentioned above, consist of significantly more episodes and recidivate more frequently than unipolar disorders. Therefore, in bipolar schizoaffective disorders the number and frequency of cycles (a cycle is the time period between the beginning of an episode and the beginning of the next episode) is higher. The length of episodes depends on the therapeutic success within an episode, on its form - whether it is currently depressive, manic, or mixed -, on whether there is a schizo-dominating symptomatology and on whether persistent alterations (residual states) occur : mixed episodes, schizo-dominated forms and the occurrence of persistent alterations seem to predispose for longer episodes.[4,35)]

In about two thirds of patients, schizoaffective disorder shows several types of episodes during course - it is polymorphous.[4,36,37)] This means that they do not only have schizoaffective episodes but also pure mood or schizophreniform episodes or episodes of acute and transient psychosis. One third of patients have a monomorphous course (only one type of episode).

Polymorphism and syndrome shift between schizophreniform, mood and schizoaffective episodes during long-term course of schizoaffective disorder give reason to assume a genetically determined psychotic continuum, expressed by various manifestations that can be ascribed to the coexistence of genetic dispositions for both prototypes (schizophrenia and mood disorder).[30)]

Long-term course : One of the best approved findings is that residual states (or persistent alterations) occur significantly less frequently in schizoaffective disorders than in schizophrenia, but more frequently than in pure mood disorders.[4,5,38-40)] Although the frequency and kind of residual states and their social consequences depend on the population investigated and on definitional and methodological aspects, the following general statements can be made : In more than 50% of schizoaffective patients, symptoms remit sufficiently even after long-term course. Only 20% of the patients experience medium or severe subjective impairment or symptoms and another 25% suffer from light to moderate symptoms (Fig. 3). Residual symptoms occur much later than in schizophrenia but earlier than in mood disorders. More than half of the patients with schizoaffective disorder show good social adaptation according to the WHO criteria, even if they have been suffering from the disorder for a long time. About 75% of them are still able to work (yet 15% of them with some limitations). One quarter of working patients must give up their job due to their disorder. A large proportion of patients with schizoaffective disorder (80%), however, can still live on their own and can care for those depending on them, even after a long-term course of their illness (compared to about 40% of patients with schizophrenia, see).[4)]

Summarizing the prognosis of schizoaffective disorder it can be said that it is more favourable than that of schizophrenia, but less favourable than that of mood disorder. Hence, schizoaf-

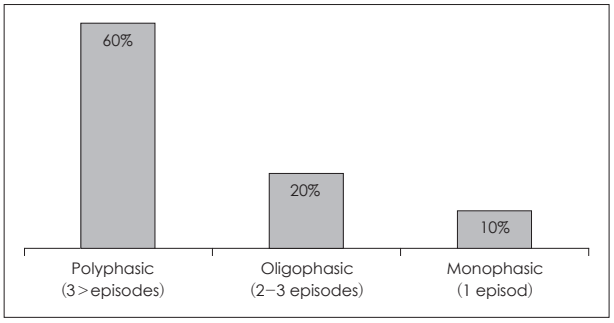

Fig. 2. Course of schizoaffective disorder.

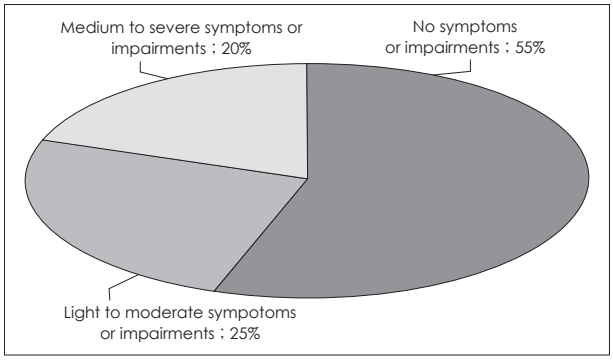

Fig. 3. Outcome of schizoaffective disorder.

fective disorder occupies an intermediate position between schizophrenia and mood disorder.

Suicidality : Suicidality is one of the biggest problems in schizoaffective disorder. When considering only schizodepressive episodes, suicidality appears to be even higher than in pure mood disorders. Taking into account the total suicidal symptomatology - suicidal thoughts, suicide attempts and committed suicide - it must be noted that more than two thirds of patients with schizoaffective disorder develop suicidal symptoms at least once during long-term course.[41-43] Apparently it is the combination of melancholic hopelessness and psychotic subjection characterizing schizodepressive episodes that are an important risk factor.[43] According to epidemiological studies, about 12% of schizoaffective patients die by suicide - a proportion similar to that in mood disorders.

Treatment and Prophylaxis

Although the clinical relevance of schizoaffective disorders is meanwhile well established and beyond doubt, their treatment has received less attention in pharmacological double blind studies than other psychotic or non-psychotic major mental disorders. One of the main reasons might be the problem of their definition and, most important for the pharmaceutical industry, the fact that schizoaffective disorder usually requires a combination of antipsychotics, antidepressants and mood stabilizers. Pharmacological studies dealing with schizoaffective disorder mostly investigated it as a subgroup of schizophrenia, seldom as a subgroup of mood disorders and even more seldom as a separate entity. Pharmacological studies only on schizoaffective disorder are rare. Nevertheless it can be said that schizoaffective disorder is the domain of antipsychotics and mood stabilizers.[44-48]

All antipsychotics seem to be efficient in the treatment of schizoaffective disorder, but some atypical antipsychotics like olanzapine, quetiapine, risperidone, or ziprasidone are superior or have some advantages in comparison to typical ones.[46,48] The heterogeneity of the studies and the investigated populations do not permit a science based statement on the topic. The clinical effectiveness of mood stabilizers like lithium, carbamazepine or valproate was reported in some, however, heterogeneous studies.

Pharmacotherapy varies according to the type of schizoaffective disorder. In the schizo-dominant type, the main medication must be an antipsychotic one. In the affective-dominant type, mood stabilizers and antidepressants or antipsychotics are effective. The bipolar type is treated with antipsychotics combined with mood stabilizers, whereas the unipolar type needs to be treated with antipsychotics and antidepressants. The sequential type is totally ignored in studies. Its treatment focuses on the treatment of the particular episode.

Clinical studies also reported a positive effect of electroconvulsive treatment.[49] Other treatments like augmentation with l-thyroxine found only small benefit.[50] The role of psychological treatment in schizoaffective disorder has not yet been systematically investigated.

The longitudinal treatment of schizoaffective disorder is a prophylactic one, mainly with mood stabilizers and antipsychotics.[45,47]

Differential Diagnosis

The differential diagnosis of schizoaffective disorder is not easy as it combines symptoms of several disorders. In psychotic depressive, manic or mixed episodes, hallucinations that might exist are congruent to the modified mood of the patients (synthymic). Yet, after especially DSM-IV had accepted even mood-incongruent symptoms in psychotic depression, mania or mixed states, differential diagnosis has become even more difficult. It has to be made according to the criteria described at the beginning of this paper. Psychotic depression, mania or mixed states with mood-incongruent psychotic symptoms, however, should better be allocated to schizoaffective disorders.[51]

Depressive symptoms are not rare in schizophrenia. The depressive symptomatology, however, does not meet the criteria of major depression. So-called *"postschizophrenic depression"* or *"postremissive fatigue syndrome"* can be differentiated from schizoaffective episodes by their occurrence after the schizophrenic episodes have remitted and by the fact that they do not meet the criteria of major depression. *Maniform symptomatology in schizophrenia* can be characterized by hyperactivity or euphoria but does not meet the criteria of a manic episode. *"Cycloid psychosis"*, or "acute and transient psychotic disorder" defined by ICD-10 in its category F 23, has nothing in common with schizoaffective disorder. Nevertheless, some may mix them up. This is an acute, short-term psychosis with a favourable outcome and does not combine schizophrenic and mood episodes (for a more detailed description see).[5]

Conclusion

Schizoaffective disorders are a nosological nuisance but a

clinical reality. A lot of people are affected : 20 to 30% of all so-called "endogenous psychoses" seem to be schizoaffective. Schizoaffective disorder is a life-long disease that is accompanied by high suicidality. Although therapy is more complex than that of "pure forms" such as schizophrenia or mood disorders, their prognosis is much better than that of schizophrenia, but not as good as that of mood disorders. The course of schizoaffective disorders usually is polyphasic and they require life-long attention.

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