THE PSYCHIATRY LETTER

Table of Contents

Please send your questions and comments to info@psychiatryletter.org

Schizoaffective illness

This issue examines the clinical conundrum of schizoaffective illness. Is it a legitimate diagnosis? Does it reflect a real illness? How does it relate to schizophrenia and affective illness?

Clinicians frequently face patients with the clinical picture of schizoaffective illness. In this issue, PL examines what it means. The main conclusion drawn is that schizoaffective illness, when truly present, reflects the chance comorbidity of schizophrenia and affective illness.

As an extension of last month's issue on the diagnostic interview, Dr. Tammas Kelly provides his insights into how he approaches the diagnostic interview, with a special emphasis on the benefit of an initial self-report questionnaire.

The classic study of the month examines the Roscommon family study and its implications for the diagnostic validity of schizoaffective illness.

The drug of the month is venlafaxine and its active metabolite desvenlafaxine. The many risks and harms of this agent are discussed in detail.

As with all issues beginning January 2016, continuing medical education (CME) and continuing education unit (CEU) credits are available for the special article through the PL website.

We appreciate your continued support.

Nassir Ghaemi MD, Editor

New truths begin as heresies and end as superstitions - T. H. Huxley

CME Special Article: Schizoaffective illness

The chance comorbidity of schizophrenia and affective illness?

Introduction

Our understanding of schizoaffective disorder can be organized in five different theories. One approach holds that schizoaffective disorder is its own illness, separate from others, as appears to be the case superficially by its separate diagnostic criteria in DSM-IV. A second model holds that schizoaffective disorder represents a middle clinical picture on a psychotic continuum that extends from bipolar disorder to schizophrenia; in other words, this model rejects the Kraepelinian dichotomy of bipolar disorder and schizophrenia. A third model argues that schizoaffective disorder represents the comorbidity of affective disorders and schizophrenia, thereby maintaining the Kraepelinian dichotomy and explaining overlap symptoms as chance co-occurrence. A fourth theory views schizoaffective disorder as basically a variant of bipolar disorder, and a fifth sees schizoaffective disorder as a variant of schizophrenia.

Many clinicians unconsciously take the first approach. They assume that since "schizoaffective disorder" represents two words, and they exist on a page of paper, especially in the DSM criteria, then those two words must represent a "real" thing, a real illness in the real world, separate and apart from other illnesses. This common human conclusion flows from the assumption that once you name something, it exists. Of course we name many things that don't exist, sometimes fantasies, sometimes mere falsehoods.

In the May PL issue, we reviewed the rationale for why many DSM labels do not correspond to "real" diseases or illnesses, but rather represent social constructs of the American psychiatric profession. Separate from this fact, we should keep in mind that any diagnostic label represents only a clinical picture, first and foremost. Whether that clinical picture is a different disease or illness from another clinical picture - that's a different question.

So as we get into the discussion of schizoaffective illness, PL would like to remind readers that we are talking about a "clinical picture": we see patients who have mixtures of delusions/hallucinations along with mood. What this clinical picture means - is it a separate illness or not? - is another question.

> "[There is an] assumption that once you name something, it exists."

Phenomenology

At the level of observation, the term "schizoaffective" simply applies to those individuals with continuous psychotic and mood symptoms. Unlike mood disorders, psychotic symptoms are not brief. And unlike schizophrenia, mood symptoms are not absent. Clinically, many patients seem to fall into this overlap region. In fact, the original paper describing the occurrence of such patients with such overlap was published in 1933. Indeed, Kraepelin himself observed that a good number of patients had such overlap of manic-depressive and dementia praecox symptoms. Hence, the fact that such overlap occurs is almost universally

accepted, even by Kraepelin, who originated the idea that mood and psychotic disorders differ.

By itself, the presence of overlap doesn't invalidate the diagnoses of schizophrenia and manic-depressive illness (MDI). This is partly because phenomenology is only one of four diagnostic validators (along with genetics, course of illness, and treatment effects/biological markers). This is also partly because a difference in symptoms is not an all-or-nothing phenomenon. In other words, to say that schizophrenia and mood disorders differ in symptoms is not to say that they *never* overlap. It only means that they *usually* don't overlap. And indeed, some well-done symptom prevalence studies have shown that patients with mood and psychotic symptoms tend to differentiate into two big groups, one with mainly mood symptoms and one with mainly psychotic symptoms, although there is some overlap (Figure 1).

It is sometimes argued that the mere existence of schizoaffective disorder is a counterexample to the Kraepelinian dichotomy of schizophrenia and affective illness. As should be clear from the above considerations, this is not the case. Some overlap is expected; and symptoms are only one aspect of diagnostic validation. To refute the Kraepelinian diagnostic schema, one would also need to look at genetic, course, and treatment response data.

Genetics

If schizoaffective disorder is a separate illness in its own right, one would expect that it would breed true in families. However, almost all genetic studies are consistent in demonstrating that it doesn't breed true. Schizoaffective disorder isn't found mainly in families of persons with schizoaffective disorder. Rather, various studies suggest a unique pattern. In some studies of families of persons with bipolar disorder, there is an increased prevalence of schizoaffective disorder, bipolar type. In some studies of families of persons with schizophrenia, there is an increased prevalence of schizoaffective disorder, depressed type. And in a number of well-executed studies comparing both major groups, schizoaffective disorder is more prevalent in families of persons with schizophrenia or bipolar disorder than in control populations or than in families of persons with schizoaffective disorder.

"It is sometimes argued that the mere existence of schizoaffective disorder is a counterexample to the Kraepelinian dichotomy of schizophrenia and affective illness."

These results are consistent with a number of possibilities. In some persons, schizoaffective disorder, bipolar type appears to be a more severe variant of bipolar disorder. In others, schizoaffective disorder, depressed type appears to be a less severe variant of schizophrenia. And in still others, since it seems to run in both families of persons with both schizophrenia and bipolar disorder, only two explanations seem possible: (1) either schizoaffective illness may indeed be the counterexample to the Kraepelinian there is no dichotomy between bipolar disorder and schizophrenia; no distinction between any psychotic disorders can be made and they should all be seen as one continuum; or (2) schizoaffective disorder may simply represents the

comorbidity of having, by chance, schizophrenia and bipolar disorder (or unipolar depression) *at the same time*, just as one might have diabetes and asthma at the same time.

The genetics of schizoaffective disorder argues against the concept of a separate illness, but the four other possibilities remain open.

Course

Studies of the course of schizoaffective disorder tend to be rather consistent: the course of the illness is more severe than in bipolar disorder but less severe than in schizophrenia. Further, schizoaffective disorder, depressed type appears to demonstrate less recovery than schizoaffective disorder, bipolar type.

These findings again are consistent with the four remaining models. If there is only one continuum of psychotic illness, bipolar disorder may lie at the less extreme end, schizophrenia at the more extreme end, and schizoaffective disorder in between. Hence schizoaffective disorder might have an intermediate course. On the other hand, if it represents a comorbidity, it may be that the more severe outcome of schizophrenia is leavened by the coexistence of bipolar disorder so that an intermediate outcome would be observed in schizoaffective disorder. Further, if the bipolar type of schizoaffective disorder is a variant of bipolar disorder, it would be expected to have a worse outcome than bipolar disorder but better than schizophrenia. Also, if the unipolar depressed type of schizoaffective disorder is a variant of schizophrenia, one would expect a better outcome than schizophrenia given the more responsive affective illness factor.

In sum, the course studies are similar to the genetic studies in supporting all of the models except the concept of a separate illness.

Treatment Response

This is the least specific diagnostic validator, but it still can be useful. There are few studies of treatment of schizoaffective disorder, but it is generally thought that these patients require long-term treatment with antipsychotic agents, as in schizophrenia, and long-term treatment with either mood stabilizers (bipolar type) or antidepressants (unipolar depressed type) as in the corresponding affective disorders. Again, this treatment response pattern is consistent with all four models except the separate illness model.

"....there is no evidence that schizoaffective disorder represents a separate illness distinct from schizophrenia and bipolar disorder..."

And the answer is....

What are we to conclude? What appears most clear is that, its appearance in DSM-III through 5 notwithstanding, there is no evidence that schizoaffective disorder represents a separate illness distinct from schizophrenia and bipolar disorder. Studies of symptomatology vary, but some important and well-done studies tend to find a difference in symptoms in psychotic and affective populations that more or less falls along the lines of Kraepelin's dichotomy of schizophrenia and affective disorders. While there are overlap areas, such overlap is empirically expected in a real-world population of persons (or animals or any other grouping). Therefore, studies of phenomenology can be interpreted as leaning against the single psychosis continuum model.

If schizoaffective disorder represents a comorbidity of schizophrenia and bipolar disorder, one would expect an epidemiological prevalence that is significantly lower than the other two. In other words, schizoaffective disorder should be very infrequent, since comorbidity should not be overly frequent by chance. Clinical impressions to the contrary notwithstanding, epidemiological prevalence studies indeed demonstrate that schizoaffective disorder appears to be very infrequently diagnosable in the general community, at a level of less than 0.5%, which is much lower than accepted prevalence rates for schizophrenia (1%) and bipolar disorder (2-4%).

Three final models

These considerations suggest that the remaining three models are consistent with the available diagnostic research (Figure 2):

1. Some persons experience mainly bipolar mood symptoms, with only some excess of psychosis. These persons are diagnosable with schizoaffective disorder, bipolar type, seen as a severe variant of bipolar disorder. By and large, they need aggressive mood stabilizer treatment and perhaps somewhat less aggressive antipsychotic treatment. They have a relatively good prognosis.
2. Some persons experience mainly psychotic symptoms, with only some excess of unipolar depressive symptoms. These persons are diagnosable with schizoaffective disorder, depressed type, seen as a somewhat less severe variant of schizophrenia. By and large, they need aggressive antipsychotic treatment, and perhaps somewhat less aggressive antidepressant treatment. Their prognosis, though better than in schizophrenia, is usually only fair.
3. Some persons appear to be truly schizoaffective: they experience psychotic and affective symptoms in more or less equal amounts. This group represents the true comorbidity of schizophrenia and affective disorders, has an intermediate outcome, and requires aggressive, persistent, long-term treatment with both antipsychotic agents and either mood stabilizers or antidepressants.

"....schizoaffective disorder appears to be very infrequently diagnosable in the general community..."

If clinicians try to differentiate apparently schizoaffective patients in this manner, they will encounter these three groupings.

The PL Bottom Line

- Schizoaffective disorder isn't a valid separate illness.
- When defined strictly, it likely represents the chance comorbidity of schizophrenia and manic-depressive illness in the same person.
- When mood symptoms predominate, it represents a more severe version of manic-depressive illness.
- When delusional/hallucinatory symptoms predominate, it represents a less severe version of schizophrenia.
- Treatments should target mainly the mood, or mainly delusions/hallucinations, depending on which of the last two above variants are present.

Figure 1. Symptom overlap does not invalidate two separate illnesses

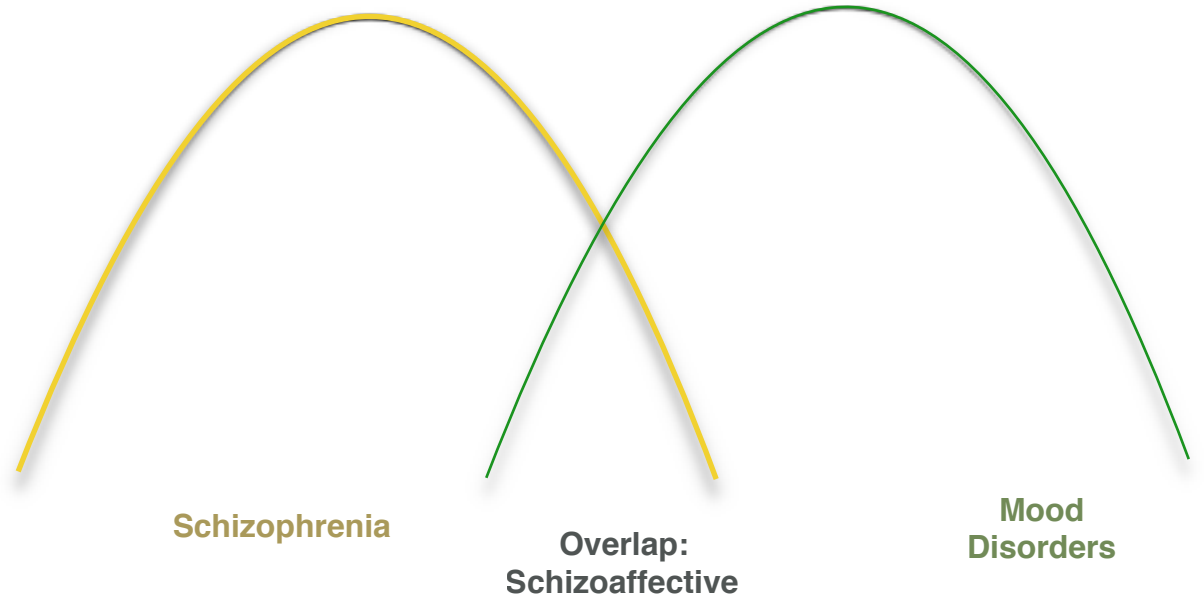
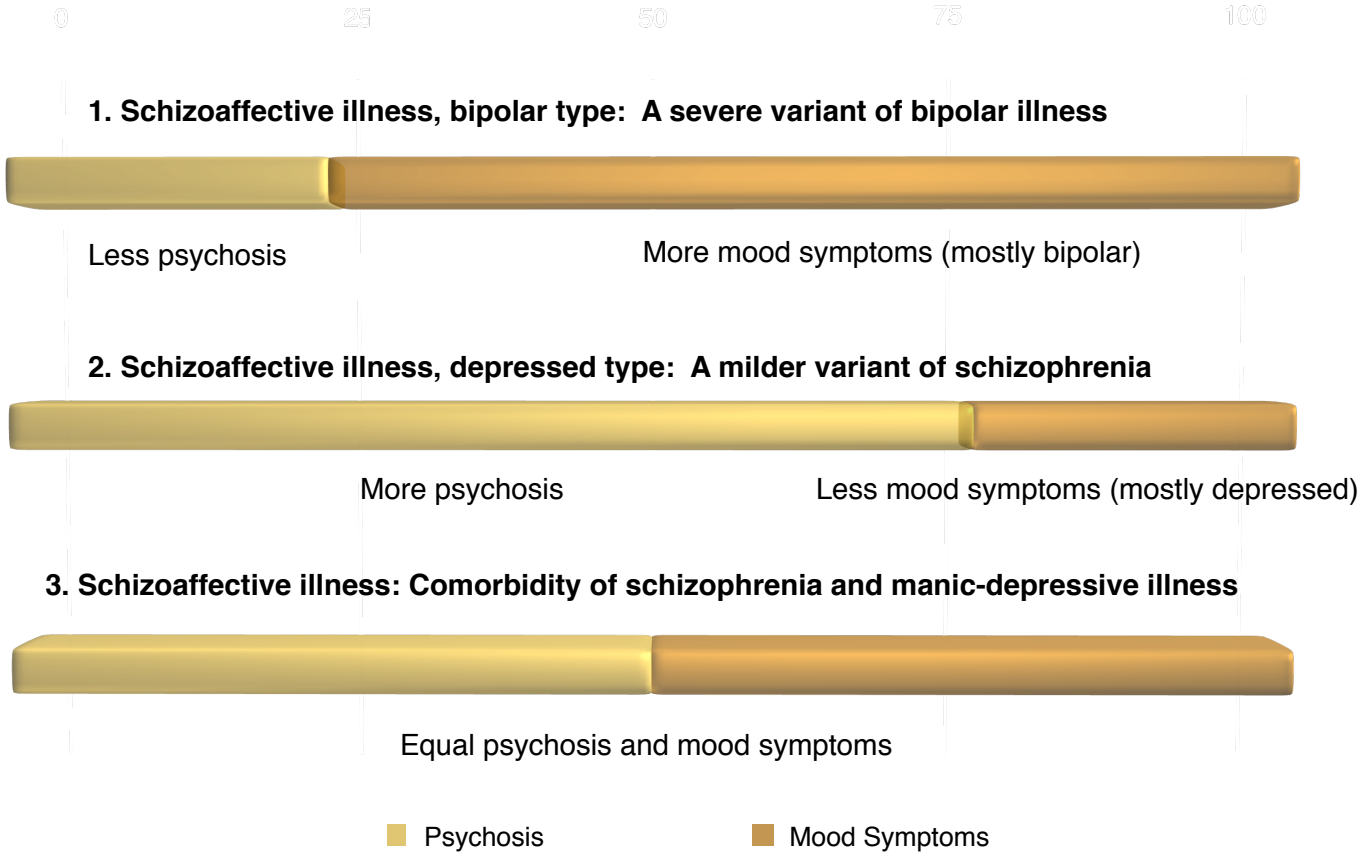


Figure 2. Three varieties of schizoaffective illness



Clinical Corner

Diagnostic interviews: Work smarter not harder

Tammas Kelly MD, Colorado

Consider how the rest of medicine makes a diagnosis: there is an initial interview followed by a physical exam. The physician will order blood tests, x-rays or some other type of diagnostic procedure. Each of these steps generates data, the latter two objective data. Unfortunately, in psychiatry we have no x-rays and it's extremely rare that a physical exam will help us make a diagnosis.

The three most important factors in real estate are location, location and location. Similarly, in making a diagnosis the three most important factors are data, data and data. The 50-minute initial interview has dominated the diagnostic process of psychiatrists since long before I became a psychiatrist 31 years ago. Historically when our biggest treatment weapon was psychotherapy, and making the correct diagnosis was less important, 50 minutes was sufficient.

When we are unsure of the diagnosis, we are supposed to schedule another appointment. If need be, we collect ancillary information from family and friends. Today the average patient acuity dictates that we make a diagnosis and start treatment by the end of the first interview. If we are to take a frank appraisal of our profession, the majority of psychiatrists will make up their mind about diagnosis in less than 50 minutes, and rarely collect ancillary information and seldom reevaluate the diagnosis even in the face of treatment failure. Economic and administrative factors (such as working for mental health clinics or hospitals) push us into limiting ourselves to 50 minutes. Sometimes it's our own arrogance.

The problem is 50 minutes is simply not long enough. Even if the patient is a good historian, it isn't long enough. For those of us who remember oral boards I don't think there was any one of us who didn't complain that 30 minutes was enough time to collect a sufficient amount of information to rule in or out the 13 most common psychiatric diagnoses, formulate a treatment plan and present and discuss the treatment plan. Oh yes we were also supposed to build rapport, collect a social history, find out about past medications, suicide attempts and hospitalizations. It just couldn't be done. If we are realistic it can't be done in 50 minutes either.

If we are unsure of the diagnosis, we are supposed to collect ancillary information from family and friends preferably at the initial appointment which just narrows that 50 minutes further.

We should have sufficient information to rule out or suspect all 13 most common psychiatric diagnoses. When was the last time you saw a "review of symptoms" in a psychiatric workup?

How then are we to compensate for this "data deficit"? We could simply lengthen the interview process and indeed psychiatrists do an 80-minute assessment. We could take two hours. However, there are many patients that can barely tolerate 50 minutes. The business maxim comes to mind. Work smarter not harder. We could borrow a page from our psychological brothers and sisters. They long ago concluded that oral interviews were insufficient to make an assessment. They collect data through a written test. In my clinic, the Depression & Bipolar Clinic of Colorado, every patient must fill out a 36-page questionnaire before they can be seen.

There are large advantages to the 36-page questionnaire. Patients have time to sit and contemplate the answers instead of dealing with the social pressure of trying to remember history, discerning the vocabulary used by psychiatrists

and answering questions while trying not to look like a loser in front of a "authority" figure. Transference is alive and well. It often interferes with the gathering of good data. Filling out the questionnaire before the initial interview decreases the transference issues. The upshot is people are generally more truthful on the questionnaire. Both because patient had to fill out the questionnaire before most transference issues start, and because the patient has committed to answers, it becomes difficult to gloss over an issue.

Diagnosing bipolar disorder has become the subject of much debate. The questionnaire has become an invaluable tool in ruling in and ruling out bipolar disorders. Verbally most previously undiagnosed bipolar patients will deny highs.

The 36 page questionnaire collects data on: demographics, current medications, current vitamins and nutraceuticals, current medical diagnoses, and ask for past medications, naming each one, its brand and generic names, its length of use, side effects, and it was stopped. The questionnaire contains screening questions for the 13 most common psychiatric diagnoses. In addition it has questions about caffeine intake, sleep history, history of head injuries, sleep apnea, hospitalizations both medical and psychiatric, suicide attempts, PMDD, demographic information, employment history and family history. Family history means addresses each relative, names most psychiatric diagnoses, and asks about the presence of psychiatric symptoms.

Patients have a hard time remembering all the medications they have had in the past. I present them ahead of time a full list of psychiatric medications, both brand and generic, and the patient at leisure (without the social pressure of trying to remember names in front of a doctor) can, with the visual clue of the name of the medication, remember much more about their experience of past treatments. In an interview are you going to go through 40+ medications one by one? There are important clues that you can miss.

There are many more advantages to the questionnaire that I won't go into here. I will say that patients' reactions to the questionnaire is telling. Most are impressed saying no other psychiatrist has been as thorough. Patients who complain almost never stay in treatment. There also is a family version to gather information from loved ones.

PL Commentary:

Dr. Kelly makes some important points in his commentary on last month's PL issue and its approach to the diagnostic interview. His main recommendation is to use a written questionnaire before beginning the diagnostic interview. This way, clinicians are not starting from nothing but actually have some material to use in the course of their interview. His questionnaire is rather lengthy, and clinicians might also consider brief self-report scales as other options, such as the Mood Disorders Questionnaire, the Bipolar Spectrum Diagnostic Scale, or the Beck Depression Inventory. Many clinicians like to use the Patient Health Questionnaire (PHQ-9) as an initial screening tool. The PL view is that all these scales can be useful as screening tools if they are followed up in the diagnostic interview. The common mistake is that the scales are used in place of the diagnostic interview. In the medical setting, if the PHQ-9 is negative, then no further psychiatric evaluation is made. This is a huge mistake for many reasons, including lack of insight on the part of patients as well as stigma, which lead to false negative self-report, not to mention the panoply of possible psychiatric problems that are not captured on these scales.

Classic study of the month: *Is schizoaffective disorder valid?*

Examining the validity of DSM-III-R schizoaffective disorder and its putative subtypes in the Roscommon Family Study. Kendler KS1, McGuire M, Gruenberg AM, Walsh D. Am J Psychiatry. 1995 May;152:755-64.

There are very few such patients in the general population

In the 1990s, a classic genetic study was conducted in Roscommon County, Ireland. That area was reported to have a somewhat high prevalence of schizophrenia, so the thought was that a genetic study might have a good chance of finding familial relationships to schizophrenia and other psychotic diseases.

One analysis that was done involved the relationship between DSM-IIIR schizoaffective disorder and schizophrenia and affective illness.

Methods

This was a family study, not a family history study. It's important to recognize the difference. Most clinicians obtain family history: this means asking the patient (proband) about psychiatric diagnoses in family members. Or it might involve asking family members of the patient about psychiatric diagnoses in other family members. Rarely is the reported presence or absence of psychiatric diagnosis in other family members investigated, much less confirmed or refuted. Everything is secondhand, sometimes hearsay.

"...schizoaffective illness did not breed true..."

A family study involves actually identifying and interviewing the family members to establish the presence or absence of psychiatric diagnoses. It is not done in clinical practice, only in research.

In the Roscommon study, after initial identification of probands with schizophrenia or affective illness, 86% of their traceable living first-degree relatives were interviewed using gold-standard DSMIIIR research diagnostic interviews.

Results

In probands with schizoaffective illness, 55% had relatives with affective illness. In contrast, probands with schizophrenia only had 28% of relatives with affective illness. So it was twice as much for the schizoaffective group.

In probands with schizoaffective illness, 6% had relatives with schizophrenia. In contrast, probands with affective illness only had 2% of relatives with schizophrenia. So it was thrice as much for the schizoaffective group.

In probands with schizoaffective illness, only 2% had relatives with schizoaffective illness. Similarly, probands with schizophrenia had 3% of relatives with schizoaffective illness, and probands with affective illness had 4% of relatives with schizoaffective illness. So it was similar in all groups, and certainly not more in the schizoaffective group.

In short, schizoaffective illness did not breed true. It is not genetically specific. Instead, it reflects the presence of genetics for both schizophrenia and affective illness at the same time.

Interpretation

What does this mean? It means that the DSM schizoaffective label, although it is a word that is spelled differently than schizophrenia or affective illness, does not reflect a reality in the natural

world that is independent of schizophrenia or affective illness. It isn't a real independent illness.

That doesn't mean it isn't a clinical picture. It doesn't mean you don't see patients with mixtures of delusional and affective symptoms. It means that clinical picture does not reflect an independent disease. You can have pneumonia with a cough and high fever; you can have pneumonia without a cough and high fever. Two different clinical pictures, but not two different diseases.

"...Two different clinical pictures, but not two different diseases..."

Instead, the shared genetics of schizophrenia and affective illness allows for only two possibilities. One option is that schizoaffective illness proves that the claimed diagnoses of schizophrenia and affective illness are in fact only one illness. The problem here is that the Roscommon family study showed that, unlike schizoaffective illness, schizophrenia and affective illness bred true separately. Affective illness was somewhat more common in relatives of affective than schizophrenic probands (34% vs 28%), and schizophrenia was much more common in relatives of schizophrenia than affective probands (8% vs 2%, a four-fold relative risk). Thus, the genetic studies supported the view that schizophrenia was a different disease than affective illness.

That leaves one other option: that schizoaffective illness reflects the chance occurrence of getting the genes for both schizophrenia and affective illness in one's family.

A good line of evidence to support this chance comorbidity model is the epidemiological prevalence of schizoaffective illness.

Prevalence

It is a widely underappreciated fact that, contrary to popular clinical opinion, schizoaffective illness is rare. It is well-known that schizophrenia occurs in about 1% of the general population, and that affective illness occurs in about 10% of the general population using standard DSM definitions. In contrast, in most studies, the frequency of schizoaffective disorder is consistently lower than schizophrenia or affective illness.

If schizoaffective illness represents the chance comorbidity of affective illness and schizophrenia, one would expect that the prevalence of schizoaffective illness would be equal to the multiplied prevalence of the other two conditions. So 1% for schizophrenia multiplied by 10% for affective illness would give an expected chance prevalence of both at the same time of 0.1%. This is close to what is calculable from the available epidemiological data.

The PL Bottom Line

- The Roscommon study found that schizoaffective illness did not breed true.
- Schizoaffective patients had genetic loading for both schizophrenia and affective illness.
- General population prevalence of schizoaffective illness is lower than either schizophrenia or affective illness.
- The most defensible interpretation is that schizoaffective illness represents the comorbidity of schizophrenia and affective illness.

Drug of the Month: *Venlafaxine (Effexor) and Desvenlafaxine (Pristiq)*

Don't prescribe it for someone with heart disease

Biological mechanism

Venlafaxine has been marketed as a serotonin-norepinephrine reuptake inhibitor (SNRI), as a way to try to differentiate it from other serotonin repute inhibitors (SRIs). But in fact, venlafaxine is just another potent SRI, with some noradrenergic reuptake blockade at higher doses. It isn't the reverse: it isn't a potent noradrenergic reuptake blocker, with some serotonin reuptake blockade. In this sense, it is much more like fluoxetine (Prozac) than it is like duloxetine (Cymbalta). Fluoxetine is the classic SRI prototype, but many clinicians don't realize that it also has some norepinephrine reuptake blockade, similar in potency in fact, in animal studies, to venlafaxine. In contrast, duloxetine is a much more potent norepinephrine reuptake blocker than venlafaxine, while still having some serotonin reuptake blockade (unlike the purely potent norepinephrine reuptake blocker, desipramine).

Fast Facts: Venlafaxine

Typical dose: 150-300 mg/d (range 75-375 mg/d)

Biological mechanism: serotonin and norepinephrine reuptake inhibition

Typical side effects: sexual dysfunction, sedation

Medically important side effects: sudden cardiac death, hypertension

Clinically proven efficacy: FDA indications for MDD, panic disorder

In other words, venlafaxine is much more like other SRIs than being like classic noradrenergic agents like desipramine.

Clinical efficacy

Like other SRIs venlafaxine has proven efficacy in MDD, mostly in moderate to severe cases, not mild MDD. There are some data of more benefit with venlafaxine in hospitalized depression compared to other SRIs. However, specific randomized studies of venlafaxine in patients who failed SRIs found that venlafaxine is NOT more effective than other SRIs in that setting of treatment-resistant depression (unlike the adjunctive efficacy proven with aripiprazole and brexpiprazole).

It has few drug interactions and can be used without much concern about liver interactions, unlike some other SRIs.

Dosing

At low doses (37.5-75 mg/d) venlafaxine is more purely serotonergic and has anxiolytic effects. Its mean effective dose in the MDD studies was about 225 mg/d (with a range of 150-300 mg/d). Though it can be dosed higher, it hasn't been proven to be more effective for MDD above 300 mg/d than below that dose.

Cardiac Harms

Most US clinicians don't realize that venlafaxine is one of the most dangerous antidepressants to use in the setting of cardiovascular disease (in contrast to other agents, like sertraline, proven relatively safe in that setting). There were some cases of sudden cardiac death with venlafaxine, which were not known until some years after its introduction to the marketplace in the 1990s. Awareness of these cases led the UK regulatory body to contraindicate it in 2004 in all persons with hypertension or heart disease. After some protest from clinicians and the relevant

pharmaceutical company, the UK regulatory body revised its restriction in 2006 to restrict venlafaxine use only in persons with uncontrolled hypertension or in persons at high risk of ventricular arrhythmia.

It's well known that venlafaxine raises blood pressure. The amount of increase has been downplayed by its manufacturer, by giving a mean increase of only up to 3 mm Hg. But this average downplays the important minority of patients who have notable increases in blood pressure. In persons with hypertension, it doesn't make sense to use an antidepressant that worsens hypertension, when many other safer options are available.

Other Risks

Venlafaxine is among the worst agents for causing serotonin withdrawal syndrome, presumably due to its short half-life, which is still the case with the XR formulation. This agent also causes mania at least twice as much as is the case with other SRIs, according to randomized trials. Thus, it shouldn't be prescribed at all in bipolar depression.

Desvenlafaxine

This agent is the active metabolite of venlafaxine. Sometimes, active metabolites can have different effects then the parent drug, but this does not seem to be the case with desvenlafaxine. Except for some differences in dosing, all of the above benefits and harms apply to this agent as well.

The PL Bottom Line

- Venlafaxine is more of a standard SRI than anything else.
- It has many harms, especially major cardiac risks, and PL recommends that it not be used in patients with cardiac disease or hypertension.
- It has severe serotonin withdrawal syndrome and high risk of mania, and thus should not be used in bipolar illness.

PL Reflection

In psychiatry, you can do biology in the morning and theology in the afternoon.

Robert Daly MD
courtesy of Ronald Pies MD

The Psychiatry Letter, P. O. Box 400536, Cambridge MA 02140. Editor and Founder: Nassir Ghaemi MD. Managing Editor: Alcides Albuquerque MD. The Editorial Board can be found on www.psychiatryletter.org. A monthly independent newsletter not owned, operated, or affiliated with any organization. It receives no financial support from any source other than subscribers. Disclosures: In the past 12 months, Dr. Ghaemi has received speaking honoraria from Sunovion Pharmaceuticals. In the past 12 months, no relationships with the pharmaceutical industry exist for any other members of the PL Editorial Board. Disclaimer: The medical information provided in this newsletter is information based on general scientific knowledge and/or clinical experience. It is not specific advice intended for individual treatment of a specific patient as would be provided in an in-person professional consultation. If users need specific medical advice for specific treatment decisions, they should consult an appropriate medical professional. No warranties are given in relation to the medical information supplied.