



Henry A. Nasrallah, MD Editor-in-Chief

Many phenotypes and genotypes manifest with similar clusters of psychiatric signs and symptoms

Diagnosis 2.0 Are mental illnesses diseases, disorders, or syndromes?

A major challenge for the DSM-V committees as they revise the diagnostic "bible" of psychiatric disorders is to determine whether mental illnesses are diseases, disorders, or syndromes.

Here's how my version of Webster's dictionary defines these terms:

- Disease: A particular distinctive process in the body with a specific cause and characteristic symptoms.
- Disorder: Irregularity, disturbance, or interruption of normal functions.
- Syndrome: A number of symptoms occurring together and characterizing a specific disease.
- Let's consider 4 facts that may be relevant for this decision.

Probably not 'diseases'

No objective laboratory test can differentiate 1 psychiatric malady from another, and this lack of specificity casts doubt on the disease model. However, many documented perturbations of normal brain functions are consistent with a disorder paradigm.

Symptom overlap

The signs and symptoms of psychiatric ailments overlap considerably. Depression and anxiety share many symptoms and frequently co-occur. Bipolar mania and schizophrenia share psychotic features, cognitive deficits, agitation, suicidality, aggressive behavior, etc. The obsessions of obsessive-compulsive disorder (OCD) resemble and sometimes morph into the fixed false beliefs (delusions) of psychosis, and OCD's compulsions often characterize the behaviors of other psychiatric disorders, such as anorexia or bulimia nervosa.

Personality disorder features essentially are attenuated but enduring forms of Axis I conditions. Nearly all psychiatric illnesses have some degree of suicidality, insomnia, and addictive behavior. Posttraumatic stress disorder's symptoms recapitulate those of numerous diagnostic cat-

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From the **Editor**

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egories, such as anxiety, depression, psychosis, negative symptoms, mania, OCD, impulsive behavior, and personality changes.

Common neurobiology

Most diagnostic categories in psychiatry share some neurobiologic features, such as:

- neurotransmitter pathways (serotonin, dopamine, norepinephrine, or glutamate)
- structural abnormalities on neuroimaging (cortical atrophy, ventriculomegaly, gray and/or white matter abnormalities) or
- genetic predispositions.

Medical and psychiatric comorbidities (migraine, chronic pain, diabetes, obesity, alcohol abuse, anxiety, eating disorders, and Axis II features) occur across all major psychiatric diagnoses.

Nonspecific medications

Psychotropics approved for treating 1 condition are frequently useful for others:

• Selective serotonin reuptake inhibitors initially were indicated for depression but soon were found to have efficacy for panic attacks, social phobia, OCD, bulimia, impulse dyscontrol, and fibromyalgia.

• Atypical antipsychotics indicated for schizophrenia have been found useful in bipolar mania, treatment-resistant OCD, treatment-resistant depression, borderline personality disorder, delirium, anxiety, etc.

• Anticonvulsants indicated for epilepsy later were approved for bipolar mania and then found to have uses in alcoholism and drug abuse, aggressive behavior, impulsivity, treatment-resistant anxiety, and psychosis.

The multiple efficacies of psychiatric drug classes strongly suggest shared pharmacotherapeutic responsiveness across psychiatric diagnoses, including those without any FDA-approved medication. They also render the opinionated and uninformed criticism of "off-label" prescribing practices hollow, effete, and counterproductive.

Back to definitions

So, should DSM-V committees define diagnostic categories as diseases, disorders, or syndromes? The state of knowledge points to disorders and syndromes rather than diseases. There very well could be a specific disease within a syndrome, but many phenotypes and genotypes manifest with similar clusters of psychiatric signs and symptoms. As research identifies each syndrome's components, future DSM editions can systematically incorporate them and their specific pathophysiologies that converge into common neural and behavioral pathways.

Until neuroscience elucidates the pathogenesis of psychiatric diseases, wouldn't it make sense to recognize 4 major syndromes: mood, anxiety, psychosis, and addiction? This might prompt the FDA to approve drugs for clusters of symptoms rather than for arbitrarily defined diagnostic categories that appear distinct but in fact share many signs and symptoms.

Psychiatrists, then, could reconceptualize how primary and secondary psychopathologic *disorders* can produce common symptoms that do not constitute a specific *disease* but do aggregate into treatable *syndromes*, the underpinning of which may be shared biological mechanisms.

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