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# Diagnosing the DSM: Diagnostic Classification Needs Fundamental Reform

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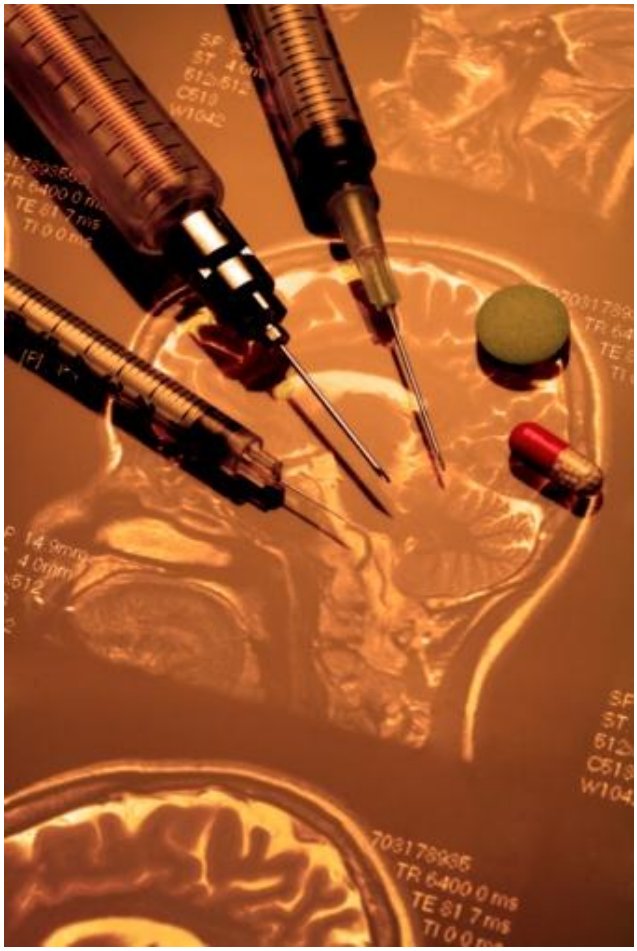

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*Editor's Note: If all goes as planned, the American Psychiatric Association will release a new* Diagnostic and Statistical Manual of Mental Disorders *(DSM-5) in May 2013. Since 1980, the DSM has provided a shared diagnostic language to clinicians, patients, scientists, school systems, courts, and pharmaceutical and insurance companies; any changes to the influential manual will have serious ramifications. But, argues Dr. Steven Hyman, the DSM is a poor mirror of clinical and biological realities; a fundamentally new approach to diagnostic classification is needed as researchers uncover novel ways to study and understand mental illness.*

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**Author's disclaimer: I have written this piece to argue my individual views. These do not represent official views of the DSM-5 Task Force, of which I am a member, or of the International Advisory Group working on the International Classification of Diseases (ICD-11) chapter on Mental and Behavioral Disorders, which I chair.**

Writing in Cerebrum (October 2009), distinguished psychiatrist Paul McHugh noted that the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) "aims only to enhance diagnostic consistency. It does not speak to the nature of mental disorders or distinguish them by anything more essential than their clinical appearance. Not a gesture does it make toward the etiopathic principles of cause and mechanism that organize medical classifications. …"[1]

McHugh's diagnosis of the core limitation of the DSM-IV (first published by the American Psychiatric Association in 1994) is absolutely correct. No sensible person could disagree. The challenge, however, is not so much the diagnosis as the cure. Many of the scientific advances that will be needed to understand the neurobiological underpinnings of mental disorders remain in the future. The DSM-IV is so deeply ingrained in the practice of psychiatry, psychology, and general medicine that it codifies mental disorders not only for patients, families, and clinicians, but also for insurance companies, regulatory agencies (such as the U.S. Food and Drug Administration), the justice system, school systems, and others. Any substantial change to the DSM system must be carefully managed to avoid many serious disruptions.

Since the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III), released by the American Psychiatric Association in 1980, the diagnosis of mental disorders has been based entirely on clinical descriptions: lists of symptoms, their duration, timing of onset, and the like. Motivated as much by the desire to elide the deep theoretical divisions (e.g., between psychoanalysts and psychopharmacologists) that had existed among clinicians for much of the 20th century as by the recognition that the underlying science was fragmentary at best, the DSM-III, DSM-IIIR ("R" for "revised"), and DSM-IV have eschewed explicit references to possible causes of illness or to pathologic processes, whether at the psychological or neurobiological levels.

Although there has been enormous progress in neurobiology during the past decade, the problem for those hard at work on the DSM-5 remains the stubborn difficulties of the science. The attempt to understand the workings of the human brain and to learn exactly what goes wrong to produce mental illnesses must number among the most challenging problems scientists have ever faced. Although, for example, the DSM-5's writing is well under way, even today its authors do not have the benefit of objective medical tests for any common mental disorder. Despite the steep challenges facing modern neurobiology, psychology, and genetics in their attempts to decode the mysteries of the brain and its ills, I argue that much can be done in constructing the DSM-5 (and also the World Health Organization's International Classification of Diseases, 11th edition, or ICD-11) that could facilitate the transition from the shallows of descriptive psychiatry to diagnoses based on cause and mechanism.

**The Benefits of Shared Diagnostic Criteria**

Despite the limitations we see so clearly in hindsight, the publication of the DSM-III in 1980 represented a major advance. Earlier editions of the DSM had provided lists of mental disorders but no guidance as to how a clinician was to make these putative diagnoses. Even where objective diagnostic tests exist in general medicine, as for hypertension or iron-deficiency anemia, explicit guidance is needed, such as for translating a specific set of blood-pressure readings into a diagnosis and treatment recommendations. Lacking objective tests, clinicians varied widely in their diagnosis of mental disorders before the DSM-III, and diagnoses also differed among countries where different diagnostic practices predominated. For example, it appeared in the 1950s that schizophrenia might be twice as common in the U.S. as in Great Britain, but the true difference was that in Great Britain, schizophrenia was understood only as a chronic condition; in the U.S., "acute schizophrenia" also was diagnosed. As new drug treatments began to emerge in the second half of the 20th century, however, it became critical to be able to match patients with the most appropriate treatment—to separate schizophrenia from bipolar disorder, for example, because the latter responds to lithium, whereas schizophrenia typically does not.

A pressing need thus emerged to address the lack of inter-rater reliability (often shortened to "reliability"). Inter-rater reliability means that two different trained raters, whether clinicians or researchers, using the diagnostic system are highly likely to reach the same diagnosis for a given patient. The solution that scientists embraced in the DSM-III was to develop and promulgate diagnostic criteria (rules) that were explicit and straightforward to apply based on observations of patients or questions that patients or family members should readily be able to answer. Thus, for example, the DSM-III defined schizophrenia as a chronic disease by explicitly basing the diagnosis on a requisite six months of active illness. As a result, the prevalence of schizophrenia was recognized to be equivalent on both sides of the Atlantic. Similarly, beginning with the DSM-III, major depression was diagnosed only if at least five out of a list of nine symptoms were present for at least two weeks.

**The Downside to Standardizing Diagnoses Early in Scientific History**

The DSM-III did yield significant progress toward inter-rater reliability, although the lack of objective tests keeps reliability far from perfect. Under the surface, however, lurked a different problem: validity. Lacking the necessary scientific information, DSM-III diagnoses were, perforce, the products of expert consensus, not the result of deep scientific understanding. In fairness, neither the DSM-III nor any of its successor manuals claimed that the diagnoses contained therein represented replicable abnormalities of anatomy, physiology, or biochemistry within the brain or provided information about the causes of the patient's symptoms. The most careful thinkers have always understood that DSM-III diagnoses should be understood as useful placeholders pending advances in research. However, this "validity problem" is often pushed into the background as a pragmatic matter. Paradoxically, the very success of the DSM system in improving diagnostic agreement among clinicians and across countries required widespread acceptance, a development that might not have occurred if users saw the DSM-III as merely heuristic.

As I have argued elsewhere, however, worldwide acceptance of a scientifically immature system has come at a price.[2] Clearly, it is important that a schizophrenia treatment study performed at one center is applicable to patients diagnosed with

schizophrenia at another. However, the entrenchment of the DSM system has had the unintended consequence of suppressing important avenues of scientific investigation. What has happened? Clinicians rely on DSM-IV diagnoses to get reimbursed by insurance companies. Scientists must generally use DSM-IV criteria to obtain research grants or to have papers accepted by journals. The pharmaceutical industry must use DSM-IV criteria in selecting patients for clinical trials in order to obtain regulatory approval for a new treatment. Psychiatrists and psychologists must memorize DSM-IV criteria for licensure exams. As a result, the DSM-IV is often treated more like the periodic table of elements than as a highly useful but limited product of expert committees working in the United States in the late 1970s—before the advent of modern molecular genetics, almost two decades before the first functional magnetic resonance imaging study, and only a few years after neurobiology began to coalesce as an academic field.

**Limitations of the DSM-IV**

As a result of its widespread acceptance, and the *de facto* reification of its diagnostic silos, the DSM-IV exerts far too much influence on the questions that scientists can ask and, in practice, do ask.[2] For example, most neuroimaging studies, clinical trials, and other investigations published in mainstream journals have, almost by necessity, taken as their starting point individual DSM-IV diagnoses, such as panic disorder, generalized anxiety disorder, or anorexia nervosa. Too rarely, however, have scientists asked (or been encouraged by funders or journal editors to ask) questions about anxiety symptoms, eating-related symptoms, or other constellations of symptoms that transgress DSM constructs. Of course the replicability of research on mental disorders benefits from a shared diagnostic language. The problem with the DSM-IV, our current shared diagnostic language, is that a large and growing body of evidence demonstrates that it does a poor job of capturing either clinical and biological realities. In the clinic, the limitations of the current DSM-IV approach can be illustrated in three salient areas: (1) the problem of comorbidity, (2) the widespread need for "not otherwise specific (NOS)" diagnoses, and (3) the arbitrariness of diagnostic thresholds.

**Multiple Diagnoses, Shared Genetic Risks**

Both in clinical practice and in large epidemiological studies, it is highly likely that any patient who receives a single DSM-IV diagnosis will, in addition, qualify for others, and the patient's diagnostic mixture may shift over time. There is a high frequency of comorbidity—for example, many patients are diagnosed with multiple DSM-IV anxiety disorders and with DSM-IV dysthymia (chronic mild depression), major depression, or both. Many patients with an autism–related diagnosis are also diagnosed with, obsessive-compulsive disorder and attention-deficit/hyperactivity disorder. The frequency with which patients receive multiple diagnoses far outstrips what would be predicted if co-occurrence were happening simply by chance. Researchers who have made careful studies of comorbidity, such as Robert Krueger at the University of Minnesota, have found that co-occurring diagnoses tend to form stable clusters across patient populations, suggesting to some that the DSM system has drawn many unnatural boundaries within broader psychopathological states.[3] Kenneth Kendler of Virginia Commonwealth University, who has performed twin studies designed to discover genetic influences on disease risk, has found that the DSM-IV disorders that frequently co-occur with each other may do so as a result of shared genetic risk factors.[4] In addition, emerging technologies in genomics and molecular genetics have begun to identify shared "disease risk genes"—better described as variations in DNA sequences that correlate with illness—across multiple DSM diagnoses. For example, DSM-IV schizophrenia and bipolar disorder appear to share a large number, although not all, of their genetic risk factors. One significant divergence is that the genomes of many people with schizophrenia, but not bipolar disorder, may harbor disease-associated duplications and deletions of large DNA segments.

Shared genetic risk factors do not refute the existence of patients with "classical" schizophrenia or bipolar disorder who would have differing treatment responses and different outcomes. What the genetic findings do suggest, however, is that the DSM-IV handling of each disorder as a discrete natural category, discontinuous from other categories of disorder and from health, is palpably wrong. The sharing of genetic risk factors is reflected in clinical populations; more patients have mixed symptoms of schizophrenia and of mood disorders than have pure DSM-IV disorders. Some of these

intermediate patients meet DSM-IV criteria for "schizoaffective disorder," a rather strange chimeric diagnostic construct, but many do not; many such patients exhibit changing symptom patterns during their lifetimes. For these and other disorders, it appears that a purely categorical approach to mental disorders fails to capture the realities of either clinical practice or laboratory science. Much psychopathology would be better represented in terms of quantifiable dimensions analogous to those in hypertension (in which the dimensions are systolic and diastolic blood pressure) or diabetes mellitus (in which quantitative measures include serum glucose and hemoglobin A1c). In a system with underlying dimensions, schizophrenia might be diagnosed in patients with elevated scores on symptoms scales that measure psychosis, cognitive disorganization, and deficit symptoms. Those patients with mixed symptoms would also have abnormalities on scales of negative or positive mood states. These patients would no longer be diagnostic orphans (who fall outside DSM-IV's narrow categories); they would be more amenable to study, and ideally they would benefit from the development of new treatments.

**"Not Otherwise Specified" and Arbitrary Diagnostic Thresholds**

The overriding focus on reliability led the authors of the DSM-III to produce highly specific criteria. Unfortunately, in many domains of psychopathology, these criteria pick out small islands in a sea of patients who do not quite fulfill the diagnostic criteria—such as many patients with symptoms of both psychosis and mood disorder. These patients may receive a diagnosis of "psychosis NOS," or psychosis not otherwise specified. In some areas of practice, such as eating disorders and autism spectrum disorders, a majority of patients may receive NOS diagnoses. This observation, like the problem of comorbidity, points to categories being far too narrowly drawn, unable to capture the full range of symptoms and severities in diagnostic spectra (as in autism) or of complex or shifting symptom patterns (as is typical of eating disorders).

Finally, the categorical system means that a disorder is either absent or present. One needs five of nine symptoms for two weeks to qualify for major depression, but someone with only four of the symptoms, of high severity, may be more impaired than someone else with five, six, or seven. Despite much research, scientists have failed to identify any natural "cut point" for the diagnosis of depression—any specific point of

discontinuity with ordinary sadness. This suggests that it, too, might be better seen in dimensional terms, with treatment recommendations based on levels of impairment or distress just as treatment recommendations for hypertension are based on long-term outcomes, such as avoiding heart attack and stroke.

**Rethinking Diagnostic Classification**

The question facing the DSM-5 Task Force is how it can encourage new approaches for science—at present we are not in a position to successfully portray disorders in dimensional terms, for example. At the same time, the task force must respect the influence of the DSM-IV and not create a premature revolution that might return us to a pre-DSM-III state that lacks a shared diagnostic language. How can we give the research community not only permission but also encouragement to rethink the classification of psychopathology? How can we encourage scientific innovation while ensuring that clinicians can still communicate with patients and families—and also with insurance companies, schools, and courts?

The approach for which I have argued is to focus the major efforts of the DSM revision not on individual diagnoses but on the assembly of larger clusters that could facilitate the application of modern neuroscience, psychology, and genetics to the understanding of mental disorders.[2, 5] Lest that seem far too abstract: Simple phobia, social phobia, panic disorders, and generalized anxiety disorder would continue to be found in the DSM-5. However, they would be placed in an anxiety disorders cluster. This cluster would, moreover, be situated within a larger meta-cluster termed the "emotional" or "internalizing" cluster. This meta-cluster would comprise several additional clusters: depressive mood disorders (perhaps to include major depression, dysthymia, and a proposed mixed anxiety-depression diagnosis); disorders resulting from trauma or severe experiences of adversity; and a newly recognized cluster of obsessive-compulsive disorder and related disorders (such a compulsive hair pulling or skin picking).

Scientists would be free to continue to work on individual disorders, but they would be encouraged to be agnostic about the narrow boundaries within clusters or even some of the divisions within the meta-cluster when designing new genetic, cognitive, imaging, or treatment-development studies. We also would hope that new ways of

representing symptoms within and across clusters would be tested, such as the identification of symptom dimensions, neurobiological endophenotypes (neural abnormalities that might underlie symptom productions), and the like. Some candidate clusters, such as the emotional or internalizing clusters described above, have come directly from the work on comorbidity[3] and twin studies,[4] which find that certain disorders are highly likely to co-occur. Another proposed cluster might derive from our emerging understanding of brain development. Within the DSM-5, these clusters might be represented as chapters or other major divisions. What is important, however, is not a new table of contents for the DSM-5 but a system that facilitates a fundamental and thorough reanalysis of diagnostic classification.

An important goal, without which such an effort will have little utility, is to persuade scientists, funding agencies, and journal editors to treat clusters and meta-clusters, instead of individual DSM categories alone, as valid bases for research. I would imagine that if such an effort were successful, the DSM-6 (more than a decade from now) will have far fewer individual diagnoses than the DSM-5 and will represent many disorders as intersections among symptom dimensions. It is also possible—indeed, much to be wished for—that DSM-6 diagnoses will be constrained by objective tests, such as neuroimaging and genetics.

With respect to the DSM-5, I am agnostic about the diagnostic criteria for individual conditions, such as panic disorder or generalized anxiety disorder; in the end, I am not certain that either of these categories capture nature or will even appear in the DSM-6. When it comes to individual diagnostic categories, I would recommend that the DSM-5 take a conservative approach, leaving criteria unchanged unless compelling new evidence suggests that a change would be beneficial. Whatever the ultimate approach to the DSM-5, it is critical that the scientific community escape the artificial diagnostic silos that control so much research, ultimately to our detriment.

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