Section VI: The Art of Psychopharmacology

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A New Psychopharmacology Nomenclature

An innovative textbook of psychopharmacology would fail if it continued to use false and outdated terminology for drug classes. Antidepressants are not antidepressants; antipsychotics are not just for psychosis; anxiolytics are not just anxiolytic; stimulants don't stimulate; "mood stabilizer" has no scientific meaning.

All these terms began as clinical shorthand in the 1960s for possible clinical effects of an exciting new crop of medications, most of whose mechanisms were unknown. The uneducated guesses of that era have been reified into phrases that patients and clinicians use as if they are true. In fact, half a century later, this clinical shorthand has been disproven, either as simply false, or as insufficiently clear, or sometimes as simply not meaningful scientifically. It's time to start a textbook of psychopharmacology with clear, scientifically sound terms for drug classes.

In contrast to the parroted repetition of drug class names for half a century, the psychiatric profession has been obsessed for over three decades with how to classify its diagnoses. Centered around revisions of the American Psychiatric Association's (APA) *Diagnostic and Statistical Manual of Mental Disorders* (DSM, various editions), much of this debate has been about the practical implications of how we diagnose mental illnesses. It is presumed frequently that if a condition has an official DSM diagnosis, then it will be treated more assiduously, often with medications, and, depending on whether one likes or dislikes psychotropic drugs, interest groups array themselves for or against proposed diagnostic revisions.

In contrast, the classification of psychotropic medications has been ignored until recently. The terms used for psychotropic drug classes are imprecise and misleading: "antidepressants," "antipsychotics," "anxiolytics," "stimulants." "Antidepressants" often are ineffective for many depressive conditions; "antipsychotics" are often effective

in many non-psychotic conditions; "antidepressants" are often as effective for anxiety symptoms as "anxiolytics." And the terms "mood stabilizer" and "stimulant" are devoid of scientific meaning altogether, as will be shown in this chapter.

Current psychiatric drug classification is based on clinical terms devised and popularized over half a century ago, with codification by a special committee of the World Health Organization in 1967. It's certainly time for an update.

In the last few years, the main psychopharmacology organizations in the United States and Europe (the American College of Neuropsychopharmacology [ACNP] and the European College of Neuropsychopharmacology [ECNP]) convened a task force for just such an update. The conclusions of that task force were that drug class definitions should be based on their biological mechanism, not clinical purpose. The rationale for this approach is that clinical purposes can vary and change, but biological mechanisms, once identified, are fixed.

This textbook agrees with this basic notion, but differs from the ACNP/ECNP task force approach because the latter seeks to identify drugs in great detail, based on their biological mechanisms, and, further, to connect such mechanisms to DSM-based clinical indications. Such detailed biological definitions will be too clumsy and inefficient for clinicians. Furthermore, the problem with too much emphasis on biological mechanisms is that each drug has many biological mechanisms, not just one. Serotonin reuptake inhibitors (SRIs) also are cytokine inhibitors, and clotting factor inhibitors, and nitric oxide inhibitors, and so on. How do we know which biological mechanism is the most important?

The view taken here is that biological mechanisms should be used, but in a broad and flexible way. It may turn out that some biological mechanisms that are useful for defining a drug class are not the actual mechanisms of clinical effect. For instance, tricyclic antidepressants (defined by their chemical structure) have effects on neuropathic pain that may have to do with their impact on blocking sodium and calcium channels peripherally, not their effects on norepinephrine and serotonin.

So biological mechanisms may be better than clinical definitions, but the former can lead to confusion too if overdone. Furthermore, drug class definitions should have nothing to do with DSM diagnostic definitions, because, as discussed in Chapter 16, the latter can change as well, and, more importantly, they are weak in their scientific validity. The proposed new drug nomenclature in this chapter will be based on biological mechanism, but with the broadest such definitions, both for clinical utility and for flexibility in relation to the range of specific mechanisms that each drug may have for different clinical uses.

CURRENT USAGE: FIVE DRUG CLASSES

In current usage, there are five major drug classes in the traditional psychopharmacology nomenclature: antidepressants, antipsychotics, mood stabilizers, anxiolytics, and stimulants. A major problem with current usage is that the phrases used are not accurate scientifically, and can be misleading in their uses, as described in Box 1.1.

BOX 1.1
PROBLEMS WITH THE CURRENT PSYCHOPHARMACOLOGY NOMENCLATURE

1. Based on clinical terms ("antidepressant") that are not directly related to diagnoses (different types of depression exist);
2. Therapeutically, nonspecific (antidepressants are anxiolytic; antipsychotics are antimanic);
3. Sometimes too narrow (antipsychotics can work for non-psychotic conditions; antidepressants can work for non-depressive conditions);
4. Sometimes too broad (antidepressants are ineffective for some depressive conditions);
5. Sometimes defined by the pharmaceutical industry (origin of the term "mood stabilizer");
6. Can be associated with stigma ("antipsychotic");
7. May mislead patients ("mood stabilizer" can imply not being allowed to have a range of moods);
8. May bias research ("mood stabilizers" may not be seen as "antidepressants" worthy of study for depressive conditions).

Source: S. N. Ghaemi, "A New Nomenclature for Psychotropic Drugs," Journal of Clinical Psychopharmacology: *2015;35(4). Reprinted with permission of Wolters Kluwer.*

These five classes of drugs tend to have typical corresponding diagnoses for usage: "major depressive disorder" (MDD), schizophrenia, bipolar illness, anxiety diagnoses, and attention deficit disorder (ADD). Each common class is examined in Table 1.1, along with background regarding their historical origins, secondary indications, and biological mechanisms.

As can be seen in Table 1.1, it seems to be the case in general that primary indications for the drug classes do not demonstrate more efficacy than secondary indications. Two of five drug classes had relatively consistent pharmacological structures. All but two (amphetamines and sedating agents) had relatively consistent biological mechanisms.

This analysis finds that a drug's biological mechanism is the most consistent method for classifying psychotropic medications. The two exceptions involved either pharmacological structure (amphetamines) and/or clinical effect (sedating agents).

A NEW NOMENCLATURE

Table 1.2 provides an alternative nomenclature based on broad biological mechanism. These mechanisms apply to all drugs in each class, although subclasses and specific agents may differ from each other in having or not having other mechanistic effects.