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What's in a Name? Moving to Neuroscience-based Nomenclature in Pediatric Psychopharmacology

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Our traditional names for psychotropic medication classes lead to unnecessary confusion. As clinicians, we have grown comfortable with idiosyncratic names of psychotropic medications and forgotten how unclear and misleading they can be. For example, evidence shows that serotonin reuptake inhibitors help in pediatric anxiety disorders, but a parent with an anxious child might ask, "If you diagnosed my son with separation anxiety, why are you giving him an antidepressant?" Another parent might object to the use of a "stimulant" medication, "My daughter never slows down, the last thing she needs is a stimulant!" Similarly, an "antipsychotic" can be prescribed on-label to youth with mania, bipolar depression, tics, or irritability in autism but families and patients might be confused by or object to the implied label of being "psychotic". Further, patients or family members may

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not feel comfortable asking clarifying questions and simply do not return for follow up---concluding that the provider does not understand their child.

The current psychotropic nomenclature is largely based on concepts and knowledge from the 1960s and 70s. In many cases, the first identified psychotropic effect became the preferred term. “Stimulants” promote wakefulness. “Antidepressants” improved mood. In other cases, names evolved until sticking on the most unique effect. “Major tranquilizers” became “antipsychotics”. Other class names, such as benzodiazepines and tricyclic “antidepressants”, were named based on their chemical structure. None of these terms reflect contemporary scientific knowledge of how these medicines act in the central nervous system. For example, “antidepressants” do not bind to ‘depression receptors’ to reverse them. Instead, they block monoamine transporters, with downstream effects. Further, noradrengic ‘antidepressants’ are only effective in treating depression, while serotonergic reuptake inhibitor ‘antidepressants’ are effective for depression and OCD (Zohar et al., 2015, Locher et al., 2017). In fact, despite being labeled antidepressants, SSRIs and SNRIs, have a more favorable number needed to treat for disorders than depression (Jane Garland et al. 2016).

Beyond being out-of-date and inaccurate, the current psychotropic medication names adversely affect patient care. These names conflate diagnoses and targets of treatment. They contribute to stigma by aligning the medications (and patients) with specific disorders. “Antipsychotics” are a clear example. This class of medication has indications for depression, mania, aggression, irritability, tics, as well as psychosis (Pillay et al., 2017, Correll et al., 2011).

This issue is present beyond psychiatry. General medicine struggles with similar confusion. For example, beta-blockers are often considered anti-hypertensive medications despite having a litany of other indications such as heart failure, essential tremor, migraine prophylaxis, arrhythmias, and even anxiety. To address this, an internist treating heart failure would avoid describing a beta-blocker as an anti-hypertensive to prevent confusion that the mediation is for blood pressure control. In psychiatry, the consequences of medication class misnomers are more problematic, particularly for children. Young children can be concrete in their understanding of medicines and may not be able to separate the name of the treatment from their diagnosis, believing they must be “depressed” if they are taking an “antidepressant”. Further, well-meaning parents may attempt to explain a medicine after the visit is complete, raising the risk that the name of the medicine’s class becomes a substitute for an appreciation of the target symptoms.

Our legacy naming is problematic from a clinician’s point of view as well. Generalized naming overshadows the distinctions between mechanisms of action. Under the current nomenclature, bupropion, mirtazapine, duloxetine, and fluoxetine are all “antidepressants”; however, they vary wildly in their mechanisms of actions, side effects, and indications. In particular, some “antidepressants,” such as serotonin reuptake inhibitors, are commonly used for anxiety; whereas others, such as bupropion, have no apparent benefit for anxiety. Further, when our naming fails to distinguish medicines, it is hard for patients to understand why one “antidepressant” should work after another has failed. Promoting a more nuanced

understanding for psychotropic medications provides better differentiation for both clinicians and patients when considering, initiating, and continuing treatments.

Concerned by the limitations of our current nomenclature in the context of our growing neuroscience knowledge, a group of international organizations created a Nomenclature Taskforce to develop an approach that is rooted in scientifically-grounded neuroscience. The taskforce designed a system using current scientific data to classify psychiatric medications by pharmacology-driven nomenclature, rather than by chemical structure or disease. Instead of grouping loosely related types of medicines under the non-specific title of “antidepressants”, they are named based on their pharmacology and mode of action. This naming provides useful information for the clinician and paves the way to improved understanding for patients. It also helps to reduce stigma and misunderstanding. Instead of “antidepressants” for enuresis, clinicians can talk about “recruiting brain systems to change the depth of your sleep”. Instead of giving “antipsychotics”, clinicians can discuss “targeting the dopamine system to help you with your tics”.

The resulting system, Neuroscience-based Nomenclature (NbN), includes more than 130 psychotropic medications and also includes several layers of information beyond basic pharmacology, such as clinical, regulatory, and neurobiological data designed to help providers make informed prescribing decisions (Table 1) (Zohar et al. 2015).

As part of the classification system, the NbN expands and replaces our terminology into eleven pharmacological domains, such as Norepinephrine, Dopamine, Glutamate, and Serotonin. Ten modes of action are also identified, ranging from effects at receptors and transporters to impacts on ion channels and enzymes. These pharmacological domains and modes of action are cornerstones for a nuanced description of psychotropic medications.

Despite the many advantages to the NbN terminology, challenges exist to adopting this classification system. A primary challenge is the inertia we have as clinicians who have used the legacy nomenclature for our whole careers. However, pushing past this inertia has significant benefits. For example, when providing psychoeducation about ADHD, explaining the etiology of ADHD in the context of the dopamine and norepinephrine systems logically flows into a discussion of medication treatment---methylphenidate and amphetamine salts as dopamine and norepinephrine reuptake inhibitors and releasers. Dropping the term “stimulant” and talking about the mechanism of action creates a more insightful, coherent and less misleading explanation.

Beyond the inherent barrier of changing how we talk about medicines, another challenge is that our understanding of medication mechanisms and molecular pharmacology remains incomplete. This issue is most clearly evidenced by lithium, which currently sits in a category of its own because its exact mechanism remains uncertain despite established actions on various enzymatic targets (Mota de Freitas et al., 2016). However, despite this challenge, NbN is an improvement over lumping lithium with valproic acid and lamotrigine as “mood stabilizers”, as if their pharmacology had anything in common.

As part of NbN’s goal to be current and accessible, a free app (NbN) is available for common mobile device platforms--- including full descriptions of psychotropic medications,

their former terminology, pharmacology targets, modes of action, approved indications, efficacy (off-label use), side effects, practical notes and neurobiology. A separate child psychiatry specific app (NbN-ca) has also been developed. Different from the adult NbN app, it includes specific child-based dosing information as part of the practical notes. It also includes data on age of approval by major regulatory agencies. Through these apps, the NbN is a living document that can easily be updated and improved as new information becomes available.

The adoption of neuroscience-based nomenclature represents an opportunity for growth and improvement in our field's descriptions of the primary biological treatment when using psychopharmacology. This system offers a less stigmatizing, more scientifically grounded, easily updatable, and nuanced understanding of our treatments. Concurrently, it exposes the complexity and limitations of the field's knowledge of psychopharmacology. However, this problem is also an opportunity for improved education of our patients and ourselves. We can use these new terms to empower youth and families to better understand what their treatments do, without a distracting legacy of misnomers.

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Table 1:

Layers of information in NbN system

Characteristic		Example: Methylphenidate
1	Mode of Action	Reuptake inhibitor (DAT, NET), releaser (DA, NE) New Terminology
2	Pharmacology Domain	Dopamine, Norepinephrine
3	Approved indications	Attention deficit hyperactivity disorder in children >6 years old and adults (FDA, EMA)
4	Efficacy	Reduces signs and symptoms of attention deficit hyperactivity disorder in adults and children; Used to treat narcolepsy
5	Side Effects	Headache, insomnia, nervousness, decreased appetite.
6	Practical notes	(d) enantiomer used less often than the racemic mixture. A number of slow release formulations are available with longer durations of action (usually once daily) and lower abuse liability
7	Former Terminology	Stimulant
8	Neurobiology	**Neurotransmitter effects preclinical** Blocks DA transporter and to a lesser extent NE transporter **Physiological human** Promotes wakefulness, increased blood pressure and heart rate, insomnia. Increased ratings of “active/alert/energetic”, “stimulated,” “shaky,” and “jittery” **Brain circuits human** Normalizes abnormal cognitive function and associated fMRI signals in patients with attention deficit hyperactivity disorder

Source: NBN Website (https://www.nbn2.com/search#drug/70/rid/70)