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Introducing the Term "Neuroregulator" in Psychiatry

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Abstract: Despite the increasing burden of mental illness, social stigma and fears about the potential mind-altering effects of psychotropic drugs prevent most persons from seeking treatment. The problem is compounded by the high rate of diagnostic uncertainty in psychiatry and psychotropic drug labels that can be as confusing as the diagnosis. The terms "anticonvulsant" and "antipsychotic" often have little to do with what is being treated, and the replacement term "mood stabilizer" is inadequate because many patients for whom mood stabilizers are prescribed do not experience any significant mood instability. This calls for a more appropriate label for these psychotropic drugs. Anticonvulsants and antipsychotics have neuroregulatory effects, and converging lines of evidence suggest that most psychiatric disorders are rooted in an inherent hyperexcitability of the neurological system—the neurons won't shut off. Based on these observations, I propose that the terms anticonvulsant, antipsychotic, and mood stabilizer be replaced with the more pharmacologically and pathophysiologically-related term "NEUROREGULATOR." The adoption of this descriptive, user-friendly term by prescribing clinicians and dispensing pharmacists would help avoid patient confusion and improve medication compliance by helping patients conceptualize what these drugs do in the brain and how they might be working to relieve symptoms.

Keywords: Neuromodulators, Neuroregulators, Anticonvulsants, Antiepileptics, Antipsychotics, Mood Stabilizers, Major Tranquilizers, Psychotropic Drugs

1. Introduction

Despite the increasing burden of mental illness, social stigma and fears about the potential mind-altering effects of psychotropic drugs prevent most persons from seeking treatment. Among those who do seek treatment, many are non-compliant due to confusion about their diagnosis and misunderstandings about what psychotropic drugs do in the brain. The problem is compounded by the high rate of diagnostic ambiguity in psychiatry and psychotropic drug labels that can be as confusing as the diagnosis. The terms "anticonvulsant" and "antipsychotic" often have little to do with the patient's symptoms, and the replacement term "mood stabilizer" is inadequate because many patients for whom mood stabilizers are prescribed do not experience any significant mood instability. This calls for a more appropriate label for medications in this important drug class.

In general, drugs are named after one of three characteristics: their chemical structure, as in "benzodiazepines"; their pharmacological action, as in "serotonin reuptake inhibitors"; or their clinical effect, as in "antipsychotic" drugs. None of these apply to the term "anticonvulsant" in psychiatry because psychiatric disorders are not epileptiform in nature. Epileptic seizures involve a sudden surge of electrical activity in the brain that is precipitated by a hypersynchronous firing of neurons. The aberrant discharges tend to cause a disruption of the sensorium and a spreading of electrical activity from one region of the brain to another. Similarly, psychiatric symptoms appear to be rooted in a pathological hyperactivity of the neurological system. This is suggested by the observation that all of the factors that increase the risk of seizures also increase the risk of psychiatric symptoms, and, conversely, all of the factors that decrease the risk of seizures also decrease the risk of psychiatric symptoms [1]. In contrast to epileptic seizures, however, the hyperactivity in psychiatric disorders is thought to be circuit-specific rather than regional [1-4], and, because it is non-hypersynchronous, it does not disrupt the sensorium but rather tends to migrate from one circuit loop to another like a wandering tornado [1]. As it does, it causes normal brain signals to become abnormally amplified and persistent, resulting in pathological cognitive, emotional, and somatic symptoms that

tend to wax and wane in severity and meld into one another [1, 5-7]. Consistent with this hypothesis, the latest gene research links the top candidate genes for the major psychiatric disorders to neuronal hyperexcitability [8-20]. These associations suggest that neuronal hyperexcitability is the heritable vulnerability trait in psychiatric disorders.

2. Anticonvulsant Drugs

In an effort to address the confusion in nomenclature when anticonvulsants are used in psychiatry, the term "mood stabilizer" has, for the past several decades, been used in place of the term "anticonvulsant." However, this too is misleading because not all psychiatric patients for whom mood stabilizers are prescribed experience the classic highs and lows that define the primary disorder-type that they are used to treat; namely, bipolar disorder. Some patients in the bipolar spectrum experience more prominent waves of other symptoms such as anxiety, irritability, and difficulty concentrating. Also, when mood symptoms *are* prominent, anticonvulsants do more than stabilize them; they tend to normalize them. What's more, anticonvulsants such as alprazolam and diazepam are widely prescribed for patients with anxiety disorders though many of them do not experience any noticeable mood dysregulation. In such cases, the use of the term "benzodiazepine" has helped to avoid confusion; however, many patients with anxiety disorders are now being treated with non-benzodiazepine anticonvulsants [21-24], and most of those who are not treated with anticonvulsants are treated with antidepressants despite the fact that many anxiety sufferers do not experience any significant symptoms of depression. All of this points to the need to move away from a symptom-based drug classification in psychiatry.

Anticonvulsants have neuroregulatory effects, and, as previously discussed, the cognitive, emotional, and somatic symptoms that have been grouped into the various psychiatric disorders, including anxiety disorders, sleep disorders, mood disorders, schizophrenia, substance use disorders, eating disorders, premenstrual dysphoric disorder, postpartum depression, ADHD, tic disorders, personality disorders, recurrent headaches, and chronic pain, appear to be driven by an inherent hyperexcitability of the neurological system. When hyperexcitable neurons are stimulated by sensory inputs and mental processes, they overreact and fail to shut off [25, 26]. This causes the mind to race, emotions to surge, and physical sensations to become amplified, particularly when the mind is under stress [1]. Consistent with this neuropsychiatric hypothesis, the two drugs that have been used most commonly to self-medicate—alcohol and cannabis—have potent anticonvulsant effects. Also consistent with this hypothesis, most of the aforementioned disorders are highly responsive to prescription anticonvulsants [1, 5]. Anxiety and sleep disorders are highly responsive to benzodiazepine anticonvulsants, and bipolar disorder, which contains elements of most of the major psychiatric disorders, is highly responsive to non-benzodiazepine anticonvulsants and the anticonvulsant-like drug lithium [27-29]. What's more, numerous studies have found that patients with bipolar disorder are in most cases misdiagnosed with unipolar depression [30-32]. This observation, taken together with the fact that the more subtle disorders in the bipolar spectrum, such as bipolar II, cyclothymia, and cyclic depression, would be even more likely to be misdiagnosed with a unipolar depressive disorder, statistically points to the non-benzodiazepine anticonvulsants as the treatment of choice in the vast majority of patients who are diagnosed with major depression or dysthymia. Moreover, what in some studies has been diagnosed as unipolar depression has demonstrated responsiveness to anticonvulsants in both augmentation [33, 34] and single-agent protocols [4, 35]. Beyond that, both the benzodiazepine [36] and non-benzodiazepine [5] anticonvulsants have a long history of adjunctive use in the treatment of schizophrenia, and a number of anticonvulsants and anticonvulsant-like drugs are now being used in the treatment of alcoholism and other substance use disorders [37-39]. Additionally, the anticonvulsant topiramate has demonstrated benefit in the treatment of binge eating disorder [40], and the natural fall in the endogenous anticonvulsant progesterone, which theoretically unmasks an underlying neuronal hyperexcitability in women [1], is well-known to be associated with premenstrual syndrome, premenstrual dysphoric disorder, and postpartum depression [41]. Finally, the alpha-2 adrenergic agonists clonidine and guanfacine, both of which have anticonvulsant effects [42], have demonstrated benefit in both ADHD [43] and related tic disorders [44], and a variety of anticonvulsants are increasingly being used in the treatment of personality disorders [45-47], migraine headache [48], and chronic pain [49, 50]. Thus, anticonvulsants have demonstrated effectiveness in a wide range of psychiatric disorders.

Anticonvulsants work by regulating the firing of neurons. This, taken together with the evidence that links psychiatric disorders to neuronal hyperexcitability, leads to the idea of replacing the restrictive term "mood stabilizer" with the descriptive term "NEUROREGULATOR." Most patients could easily understand that *neuro* means "brain," and *regulator* means "regulate." The new term more accurately describes what anticonvulsants and anticonvulsant-like drugs do—they regulate the firing of neurons. The adoption of this new terminology by prescribing clinicians and dispensing pharmacists would help reduce patient confusion, increase medication compliance, and help overcome the long-held stigma of mental illness by helping patients conceptualize what medications in this broadly effective drug class do when they are prescribed for psychiatric purposes.

3. Antipsychotic Drugs

Although antipsychotic drugs were traditionally used to treat psychotic symptoms, they are now commonly used to treat bipolar mania, and they are increasingly being used as

an augmentation strategy in the treatment of depression whether or not psychotic symptoms are present. However, as with the use of anticonvulsant drugs in patients who do not have seizures, the use of antipsychotic drugs in patients who do not have psychotic symptoms creates uneasiness and confusion, which in turn causes patients to mistrust both the medication and the prescriber. This is unfortunate because antipsychotic drugs can help normalize mood, reduce anxiety, quell agitation, and improve sleep whether or not psychotic symptoms are present. The mechanism behind these broad therapeutic effects is theoretically the same as that behind their antipsychotic effects—they reduce circuit-specific hyperactivity in the brain [1, 51]. There is both clinical [52] and neurophysiological [53] evidence that psychotic symptoms develop when aberrant discharges from neurons in the brain's sensory processing systems either distort or mimic input from the environment. That would explain why, for instance, antipsychotic blockade of dopamine, a neurotransmitter that is involved in the processing of auditory signals [54], is so effective in reducing auditory hallucinations [52]. In addition to their antidopaminergic effects, antipsychotic drugs block the excitatory neurotransmitters histamine, norepinephrine, and acetylcholine, and they modulate a variety of serotonin receptors [51]. These inhibitory and modulatory effects would explain why antipsychotic drugs are also effective in reducing other psychotic symptoms including paranoia and delusions, which in theory are false beliefs that develop in response to neurological signals that are so intense and persistent that they are thought to reflect external rather than internal reality [1, 55]. These same inhibitory and modulatory effects could also explain the tranquilizing, mood normalizing, and antidepressant effects of antipsychotic drugs.

Considering all the potential benefits of antipsychotic drugs, the term "mood stabilizer" falls far short of accurately describing what these drugs can do. Recognition of the wide-ranging utility of antipsychotic drugs is not new. Just over a half century ago, the antipsychotic drug chlorpromazine made possible the large-scale deinstitutionalization of the mentally ill. Unfortunately, however, this caused antipsychotic drugs to become highly stigmatized, as their use became associated with some of the most severe forms of mental illness. That stigma remains and continues to be a barrier to compliance, particularly when antipsychotic drugs are prescribed for patients who have no history of psychosis. The alternative term "major tranquilizer" does not fair much better with patients, as it conjures up the dreaded thought of being chronically over-sedated. Subsuming antipsychotic drugs under the NEUROREGULATOR umbrella would help mitigate these barriers to compliance and reduce the stigma of mental illness by helping patients better conceptualize how these drugs work to relieve symptoms.

4. Conclusion

Due to the long and tumultuous history of psychiatry and the sensitive nature of psychotropic drug therapy, drug classification and nomenclature have come to have a powerful influence on public perception and medication compliance. This calls for a reassessment of drug terminology in psychiatry, particularly in light of the known pharmacological effects of anticonvulsant and antipsychotic drugs and emerging new insights into the mechanisms by which they work to relieve symptoms. Despite the well-known benefits of anticonvulsant and antipsychotic drugs in the treatment of psychiatric disorders, the term "anticonvulsant" is diagnostically inappropriate, and the substitute term "mood stabilizer" neither reflects the scope of benefits nor the pharmacological effects of either anticonvulsant or antipsychotic drugs, the latter of which are increasingly coming to be known as adjunctive mood stabilizers. That is a call to replace these discrepant terms with one that more accurately describes what these drugs do.

Based on emerging new insights into the pathophysiology of psychiatric disorders [1-7, 56], it is becoming increasingly evident that psychiatric symptoms such as anxiety, depression, and insomnia are the result of an inherent inability of neurons to self-regulate. Correspondingly, the known pharmacology of anticonvulsant and antipsychotic drugs is a regulatory one. In recognition of this, I propose that anticonvulsants, antipsychotics, and other psychotropic drugs that primarily inhibit, modulate, or otherwise reduce excitation in the brain be referred to as "NEUROREGULATORS." The use of this descriptive, pharmacologically-based new term in place of the restrictive, symptom-based term "mood stabilizer" would help avoid patient confusion and improve medication compliance by helping patients conceptualize what drugs in this broadly effective category do in the brain and how they might be working to relieve symptoms.

Competing Interests

The author declares that this article was conceived and written in the absence of any competing interests.

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