Introduction and overview: The role of anticonvulsants in psychiatry

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Anticonvulsant drugs have emerged as effective clinical tools for the treatment of various psychiatric disorders. The links between epilepsy and psychiatry have been well documented. In 1970, Japanese psychiatrists revealed that carbamazepine, considered then for use only in trigeminal neuralgia and epilepsy, had antimanic properties.[1] Since that time, knowledge of the efficacy and limitations of these drugs in psychiatric disorders has increased significantly, and will continue to do so with studies involving four new anticonvulsants—gabapentin, lamotrigine, topiramate, and tiagabine.

The goal of this symposium is to disseminate the information available about the emerging psychiatric uses of anticonvulsant agents and more specifically to provide a better understanding of the pharmacokinetics of the new anticonvulsant agents; to review the underlying rationale of anticonvulsant use in psychiatry in general and specifically in neuropathic pain and withdrawal syndromes; to compare and contrast traditional versus current treatment protocols in bipolar disorders; and to evaluate new strategies for treating panic disorder and social phobia.

Dr. Norman Sussman reviews the historic background and rationale for the use of anticonvulsants in psychiatry. He examines issues concerning the use of the new anticonvulsants, particularly gabapentin and lamotrigine, in psychiatric disorders and reviews the evolution of pharmacologic treatments for bipolar disorder, evaluating the effectiveness of currently approved medications (lithium and valproate) and conventional anticonvulsants (valproate and carbamazepine). Dr. Sussman reviews several clinical studies showing gabapentin and lamotrigine to be effective alternatives for the treatment of bipolar disorder, but cautions that additional studies are needed to determine what specific role these new agents might have in the treatment algorithm.

Dr. Harold Morris reviews the pharmacokinetics of the new anticonvulsants, felbamate, gabapentin, lamotrigine, tiagabine, topiramate, and vigabatrin. The pharmacokinetic profiles of these new anticonvulsants are significantly better than those of the conventional antiepileptic drugs—limited drug interactions make them safer and easier to use. However, with the exception of gabapentin, all these new agents have hepatically mediated drug interactions; thus, more pharmacokinetic studies are required for optimal utilization. Studies to gain insight into their mode of action may reveal new pathways, identify drug interactions, and define adverse effects. This will facilitate the establishment of appropriate treatment guidelines for their use in psychiatry.

Dr. Edward Covington reviews the use of anticonvulsants in neuropathic pain and detoxification. Anticonvulsants have been used in the treatment of neuropathic pain since the early 1940s. However, the conventional agents were generally not effective in this area. The rationale for the use of anticonvulsants in pain is similar to their rationale for use in epilepsy—that is, they suppress discharges in pathologically altered neurons. Neuropathic pain, or abnormal pain, can be best defined as a disproportion between

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the pain signals and the provoking stimulus, if, in fact, a provoking stimulus exists. Dr. Covington examines the pathophysiology of neuropathic pain and the acting mechanisms of conventional and new anticonvulsants in pain. Particular attention is given to studies that demonstrate the superior analgesic effects exhibited by the new anticonvulsants.

In addition, this article discusses the efficacy of anticonvulsants in the treatment of withdrawal symptoms occurring after the discontinuation of sedative-hypnotic drugs and alcohol. Dr. Covington reviews early clinical experiences with carbamazepine and valproate and examines recent studies of gabapentin in sedative-hypnotic withdrawal and alcohol withdrawal.

Without a thorough understanding of pain and drug mechanisms, response predictions for anticonvulsants in the management of neuropathic pain and withdrawal syndromes are limited. It is of interest, however, that the anticonvulsants that are most useful for neuropathic pain are the most effective for sedative-hypnotic withdrawal and bipolar disorder. This raises the question of whether commonality exists in these disorders, and whether neural hypersensitivity and kindling may be an underlying unifying construct.

Dr. Gary Sachs reviews current treatments and new strategies for bipolar disorder. Lithium is considered to be the standard treatment for new onset bipolar disorder. However, many patients are not able to tolerate lithium, and certain subtypes of bipolar disorder are resistant to lithium treatment.[2] Recognition of the overall limited benefits of lithium sparked interest in alternative treatments. Carbamazepine was the first anticonvulsant used for bipolar disorder in the 1970s. Thereafter, valproate became widely used and is the only medication other than lithium to be approved in the United States for treating bipolar disorder.

Emerging evidence indicates that gabapentin, lamotrigine, and topiramate hold considerable promise as adjunctive or alternative treatments in refractory bipolar disorder. This article evaluates the traditional pharmacologic approaches to bipolar disorder and the recent clinical experiences with the new anticonvulsants. The role of practice guidelines in the treatment of bipolar disorder is discussed as well.

Lastly, Dr. Jonathan Davidson reviews the current treatment options and new strategies for panic and social phobia, two areas that offer very little in clinical experience and data concerning treatment with anticonvulsants. Panic disorder is a condition that affects 3.5% of adults in the United States. The phenomenology of panic disorder, including "paroxysmal" onset and short duration of attacks, psychosensory symptoms, dissociative states, and vegetative arousal, resembles that of complex partial seizures, thus creating a strong rationale for the use of anticonvulsants as alternative treatment.

The first part of this article reviews the standard pharmacologic treatment strategies for panic disorder—tricyclic antidepressants, monoamine oxidase inhibitors (MAOIs), serotonin-selective reuptake inhibitors (SSRIs), and benzodiazepines—while considering the potential role of valproate and other anticonvulsants.

The second part of this discussion examines the treatment of social phobia, an extraordinarily common disorder. Social phobia is best defined as a pathologic fear of scrutiny by other people in social settings, with a marked and persistent fear of performance situations.

In the past, pharmacologic therapy had not been considered first-line treatment for social phobia due to problems diagnosing and defining this disorder.[3] Now that the two distinct forms of social phobia, discrete or nongeneralized and generalized, are clinically recognizable, treatment can be targeted more specifically to relieve symptoms.[3] Among the anticonvulsants, gabapentin in particular shows considerable promise in treating social phobia. Results of a 14-week, placebo-controlled, double-blind trial evaluating the efficacy and safety of gabapentin in social phobia are analyzed.

Because of their unique mechanisms of action and improved pharmacokinetic profiles, the new anticonvulsants have provided clinicians with increased treatment options for patients with psychiatric disorders. The initiation of randomized, controlled studies is warranted to clearly define the clinical spectrum of these new agents and their position versus conventional therapies. These elements will be critical in determining the direction of future research in psychopharmacology.

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