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Psychotropic Properties of Antiepileptic Drugs

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Antiepileptic drugs are important psychotropic agents. That is, they affect the mind influence behavior. In the early days of therapy with medications such as phenobarbital and phenytoin, patients and doctors were unfortunately faced with almost exclusively negative psychotropic effects. However, in the past few decades, positive behavioral effects of antiepileptic drugs were recognized. This article reviews some of the major findings, highlighting our limited medical knowledge in this critical area.

Their meteoric rise of antiepileptic drugs as therapy for psychiatric disorders outpaces evidence of their efficacy. For many drugs such as carbamazepine, gabapentin, lamotrigine, and valproate, a large percentage of prescriptions are written by psychiatrists to treat behavioral disorders. However, there are few, large randomized controlled trials on the behavioral effects of antiepileptic drugs. The best evidence supports the effectiveness of antimanic and mood stabilizing properties of carbamazepine, valproate, and lamotrigine in bipolar disorder. There is also good data to support the effectiveness of gabapentin for some cases of social phobia. However, antiepileptic drugs are used to treat a wide spectrum of other behavioral disorders ranging from depression to aggression to binge eating. Their growing off-label use in psychiatric disorders (i.e., indications that are not approved by the Food and Drug Administration) is potentially dangerous. In many cases, these drugs are used without clear evidence that they have beneficial effects. The studies that support the use of these drugs are often based on single case reports or small series or

“controlled studies” that are limited in the number of patients studied or the methodology used (may bias towards positive findings). For instance, despite numerous anecdotal reports on the beneficial effect of gabapentin in bipolar and unipolar depression, two randomized controlled trials showed that gabapentin is ineffective for these disorders. *Indeed, no antiepileptic drug is proven to be effective to treat depression.* Similarly, the negative cognitive effects of topiramate in some patients were shown in randomized controlled trials and supported by clinical observations in large epilepsy practices. Although there is no evidence from randomized controlled trials of topiramate’s effectiveness for any psychiatric disorder, its use in behavioral disorders is growing steadily. In part, topiramate’s “side effect” of weight loss often leads to its use to counteract drugs that cause weight gain such as valproate, gabapentin, and some antidepressant and antipsychotic drugs. Also, funding by drug companies for research studies and support for physicians may bias the interpretation of the data, especially in nonrandomized and uncontrolled studies, which are the most common in this area.

The mechanisms by which antiepileptic drugs affect behavior are incompletely defined. They may affect behavior via actions that suppress seizures. In general, sedative antiepileptic drugs possess anti-anxiety, antimanic, and sleep-promoting benefits, but may cause fatigue, impair attention, and depress mood. These drugs, which often enhance the activity of inhibitory neurotransmitters, include barbiturates, benzodiazepines, valproate, gabapentin, tiagabine, and vigabatrin. Activating antiepileptic drugs, such as felbamate and lamotrigine may possess antidepressant and attention-enhancing efficacy, but may cause anxiety, insomnia, and agitation. Topiramate, levetiracetam, and zonisamide have multiple CNS actions that straddle these categories. These generalizations are limited by the wide variability of clinical responses. For example, barbiturates, valproate, vigabatrin, and levetiracetam cause sedation and, in some patients, irritability and anxiety. All antiepileptic drugs can have beneficial or harmful psychotropic properties in different patients. Atypical behavioral responses to antiepileptic drugs and other medicines appear to be more frequent in children and the developmentally disabled. An individual’s behavioral response to a specific antiepileptic drug is influenced by their neurological and psychiatry history, drug interactions, genetic factors, and environmental factors. While treatment concerns individual patients,

studies identify group averages. More data are needed to predict individual responsiveness to antiepileptic drugs.

Table: Potential Psychotropic Effects of Antiepileptic Drugs

Antiepileptic Drug	Beneficial Effects	Harmful Effects
Barbiturates	Anxiety, Mood stabilizing, Sleep	Aggression, Impaired cognition & attention, Depression, Irritability, Sexual function and desire,
Carbamazepine (Carbatrol, Tegretol)	Aggression, Mania, Mood stabilizing *	Irritability, Impaired attention
Ethosuximide (Zarontin)		Aggression, Confusion, Depression, Insomnia
Gabapentin (Neurontin)	Anxiety, Insomnia, Social phobia*, Mood stabilizing,	Irritability/agitation (usually in children with disabilities)
Lamotrigine (Lamictal)	Mania*, Mood stabilization*,	Insomnia, Irritability (usually in children with disabilities)
Levetiracetam (Keppra)	?	Anxiety, Depression, Irritability (all appear more common in children)
Phenytoin (Dilantin)	Mania	Depression, Impaired Attention
Tiagabine (Gabatril)	Mania, Mood stabilization	Depression, Irritability
Topiramate (Topamax)	Binge eating, Mania, Mood stabilization	Depression, Impaired cognition (word finding, memory) & attention, Irritability
Valproate (Depakote/Depakene)	Agitation, Aggression, Irritability, Mania*, Mood stabilization*,	Depression
Zonisamide (Zonegran)	Mania	Aggression, Emotional lability, Irritability

* - Good data to support benefits