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Venlafaxine in the Treatment of Unresolved Symptoms of Depression Following Antidepressant Therapy

D.L. Dunner, MD, FACPpsych

A Review of Evidence-Based Psychotherapies for Bipolar Disorder

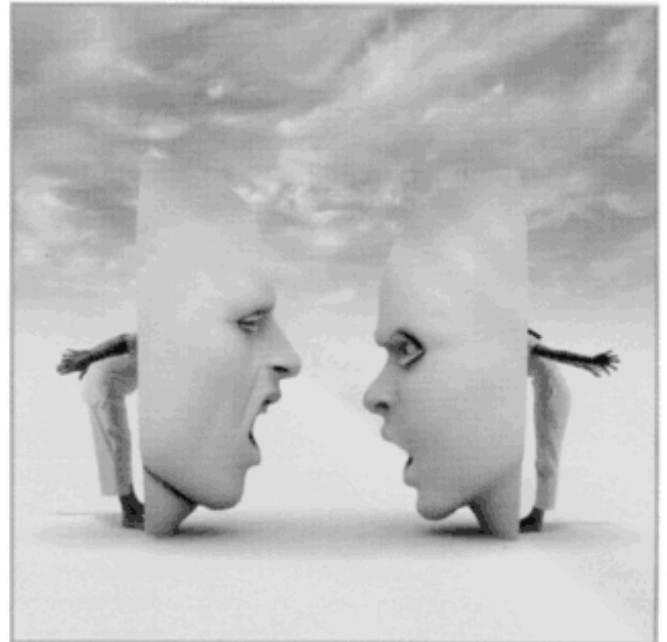
R.E. Geller, MD, J.F. Goldberg, MD

Cranial Electrotherapy Stimulation Reduces Aggression in Violent Neuropsychiatric Patients

A. Childs, MD, FAPA, L. Price, PhD

Current Approaches to the Treatment of Bipolar Disorder With Atypical Antipsychotics

E. Vieta, MD, PhD



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What Next?

Overcoming Treatment Resistance

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In this month's Primary Psychiatry, each feature article addresses an aspect of treatment involving complicated psychiatric disorders. Specifically, each article focuses on patients who do not respond to "first-line" interventions and sometimes do not respond to conventional treatments at all. In many of these cases, a therapeutic dilemma is whether to try a sequence of alternative therapies or use multiple agents, called drug cocktails. Treatment failure sometimes also leads patients to seek out alternative therapies, such as nutrients and vitamins, or procedures that have not been extensively studied for their efficacy and safety.

Given its prevalence, major depressive disorder (MDD) may be the "treatment resistant" psychiatric disorder seen most by primary care physicians and psychiatrists. Consistently, studies have shown that one third of patients fail to achieve complete resolution of their symptoms following initial antidepressant therapy for MDD, and there is no explanation for why these patients are resistant to medication. Recent evidence on the next step for clinicians after initial treatment failure has not shown that any strategy, such as switching or combining drugs, is better than any other. Nevertheless, there is a widely held belief that drugs with multiple neurotransmitter effects, such as the serotonin norepinephrine reuptake inhibitors (SNRIs), may be marginally superior to selective serotonin reuptake inhibitors (SSRIs) as "go to" drugs after initial treatment failure.

David L. Dunner, MD, provides a perspective on the available evidence for the efficacy of the SNRI venlafaxine in the treatment of unresolved depression symptoms following adequate antidepressant therapy. Dr. Dunner explains the implications of available data for achieving remission in patients with treatment-resistant depression. He concludes that, although comparative studies do not conclusively show venlafaxine to be superior to augmentation or switch strategies for patients who do not respond to an SSRI there is suggestive evidence that venlafaxine may represent a better option than staying within class. If such an advantage does exist, the question that remains is whether response with venlafaxine

is related to the drug's dual mechanism of action, which is shared by the SNRI duloxetine.

Prior to reading the article by Allen Childs, MD, and Larry Price, PhD, describing the use of cranial electrotherapy stimulation (CES) to treat 48 chronically aggressive neuropsychiatric patients in a maximum security psychiatric hospital, I had been unaware that CES was a United States Food and Drug Administration approved treatment. The early focus of CES was as a treatment for sleep disorders and the therapy was known as electrosleep therapy. In fact, several types of CES units are certified as being effective for the treatment of anxiety, depression, insomnia, and pain. I am unsure why so little is published about this procedure; CES is not cited in standard psychiatric textbooks. Yet, case reports submitted by Childs and Price were accepted for publication in a major psychiatric journal.¹ The robust antiaggressive effects of CES they report in chronically ill neuropsychiatric patients warrants publication of their findings. As in the case of electroconvulsive therapy, multiple treatments are typically needed to produce clinical effects. CES should not be confused with transcranial magnetic stimulation (TMS), an experimental procedure that is being tested at multiple academic centers. Far more research data about TMS have been published in scientific/medical journals than have the results of CES studies. Readers should keep in mind that the article by Childs and Price in this month's issue contains case reports and not

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a controlled trial. Yet, given that CES is reported to be well tolerated—headache or skin irritation at the electrode site being the most common side effects—the possibility that it may be used to reduce aggression warrants further research. Aggression represents the most potentially serious behavioral consequence in neuropsychiatric patients.

Ruth E. Geller, MD, and Joseph F. Goldberg, MD, elaborate on the role of psychotherapy in the treatment of bipolar disorder in their article on psychotherapies for bipolar disorder. These psychotherapies, used as an adjunct to pharmacotherapy, include psychoeducation as well as cognitive-behavioral therapy, family-focused treatment, and interpersonal/social rhythm therapy. Geller and Goldberg note that these therapies may improve patients' ability to cope with stress and improve insight into the reemergence of symptoms.

Bipolar disorder represents another common psychiatric disorder that is often difficult to treat. Often, it is possible to manage acute episodes of mania, hypomania, or bipolar depression but is difficult to maintain stability over time. Eduard Vieta, MD, PhD, presents an article examining the

role of these newest type of drugs as mainstream mood stabilizers. All of the atypicals have been well-studied as treatments for acute mania and some are also indicated for mixed mood states, bipolar depression, or as maintenance treatment. Since bipolar disorder invariably requires long-term treatment, Vieta notes that there is a need for well-tolerated and clinically effective maintenance therapy. It remains to be seen whether atypical antipsychotics will fill this need for long-term therapy. However, this article discusses what is known about atypicals and other drugs used to treat bipolar disorder in order to make clinicians aware of the relative risks and benefits of these interventions. In addition, the article mentions that medication alone is not sufficient to provide optimal therapeutic outcomes and that psychotherapy and psychoeducation are important in improving adherence to treatment. *PP*

REFERENCE

1. Childs A. Cranial electrotherapy stimulation reduces aggression in a violent retarded population: a preliminary report. *J Neuropsychiatry Clin Neurosci*. 2005;17(4):548-551.