

Introduction

Optimizing Wakefulness in Patients With Fatigue and Executive Dysfunction

Stephen M. Stahl, M.D., Ph.D.

Symptoms of common psychiatric disorders such as major depressive disorder (MDD) and attention-deficit/hyperactivity disorder (ADHD) are hypothetically mediated by the malfunction of different neurocircuits. When these malfunctions are incompletely addressed by pharmacotherapy, residual symptoms may persist. These symptoms often include fatigue, sleep disturbances, and executive dysfunction (demonstrated by difficulties with judgment, communication, and problem-solving, to name a few). For full remission to be achieved, these symptoms must be eliminated. This supplement reviews strategies for the alleviation of fatigue and executive dysfunction in both the primary care and clinical psychiatric settings.

First in this supplement is a brief commentary by Larry Culpepper, M.D., M.P.H., in which he explains the importance of recognizing fatigue and executive dysfunction in the primary care setting. Since the burden of diagnosing and treating mental disorders falls more and more to primary care physicians, it behooves them to be familiar with symptoms of those disorders, even the more subtle symptoms like fatigue and executive dysfunction.

In the first article of the supplement, my colleagues and I hypothesize that since the symptoms of MDD differ from one patient to another, different circuit malfunctions may be to blame. The presence of residual symptoms in many antidepressant-treated patients implies that not all circuits are successfully targeted by antidepressants. We go on to propose a new neurobiologically informed treatment strategy that targets neurotransmitters in the circuits that may be malfunctioning; this strategy should alleviate residual symptoms.

George S. Alexopoulos, M.D., then turns our attention to late-life depression, especially late-onset depression in geriatric patients. Dr. Alexopoulos posits the existence of a depression-executive dysfunction syndrome to describe the clinical presentation of late-onset depression. This syndrome has been conceptualized as a neurologic disease, and it appears to be somewhat resistant to treatment with classical antidepressants. However, agents that improve vigilance and alertness, as well as psychosocial interventions, may be effective treatments for late-onset depression.

Many patients with depression, no matter what age, experience sleep disturbances such as insomnia, excessive sleepiness, and fatigue. Karl Doghramji, M.D., describes treatment strategies that address these disturbances. He argues that both pharmacotherapy and behavior modification are viable treatment strategies.

Maurizio Fava, M.D., points out that fatigue and executive dysfunction can occur in MDD both before and after antidepressant treatment. These symptoms are often associated with untreated depression, but they can also emerge as side effects of antidepressant treatment. Augmentation strategies can be useful to manage fatigue and executive dysfunction in antidepressant-treated patients, but more research into the efficacy of these strategies is necessary.

Executive dysfunction may also play a part in the clinical presentation of ADHD. According to James M. Swanson, Ph.D., the inattention, hyperactivity, and impulsivity that characterize ADHD may be due to underlying deficits in executive function. Treating ADHD with a nonstimulant agent that improves executive function by improving wakefulness may be beneficial, although, again, further study is needed.

Joseph A. Lieberman, III, M.D., M.P.H., concludes the supplement by returning to the primary care perspective. Since executive dysfunction can present in a variety of ways—for example, tiredness, forgetfulness, poor communication, and poor decision-making skills—primary care physicians may have difficulty recognizing it. In addition to the variety of ways it manifests, executive dysfunction can be associated with a wide variety of medical and mental conditions, as can fatigue. Dr. Lieberman

From the Neuroscience Education Institute, Carlsbad, Calif., and the Department of Psychiatry, University of California, San Diego.

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Corresponding author and reprints: Stephen M. Stahl, M.D., Ph.D., Neuroscience Education Institute, 5857 Owens Ave., Suite 102, Carlsbad, CA 92009.

discusses the utility of several simple diagnostic and mnemonic tools in the differential diagnosis of both executive dysfunction and fatigue in primary care.

Fatigue and executive dysfunction are often, but not always, found together. A careful differential diagnosis is necessary to determine the ultimate cause of these symptoms, which may be the result of a psychiatric disorder such as depression or ADHD, side effects of medication,

a primary sleep disorder, or a medical condition. An agent that treats both symptoms may be useful in both psychiatry and primary care, but the stimulants currently in use are associated with high abuse rates and some untoward side effects. Newer agents that promote wakefulness hold promise in treating fatigue and executive dysfunction and may prove to be effective without those additional concerns.