Advancing the Treatment of Anxiety Disorders: New Findings and Novel Uses for Atypical Antipsychotics

By Charles B. Nemeroff, MD, PhD

Anxiety disorders are among the most prevalent and disabling psychiatric diagnoses in our society, yet in many ways they remain among the least well-understood of the major mental illnesses. The anxiety disorders are an open avenue for investigation across many different domains of basic science and clinical research, particularly in the areas of vulnerability and resilience, treatment refractoriness, special populations, and discovery of novel therapeutic approaches. This publication reviews new findings in the field of anxiety disorder research with an emphasis on the environmental and neurobiological basis of vulnerability and the unmet needs in treatment.

One of the most exciting and forward-thinking avenues of current investigation in the anxiety disorders relates to risk factor research. A growing body of literature from the diverse fields of functional neuroimaging, non-human primate and rodent behavior and neurobiology, and clinical trauma research is converging to suggest that severe adverse experiences in young children have a profound and lasting effect on the developing brain. Early-life adversity can permanently change elements of neural circuitry, particularly the corticotropin-releasing factor (CRF) system, and result in abnormalities in the stress response and an increased risk for development of mood and anxiety disorders later in life.

Much work remains in the clinical arena, despite a seemingly ample body of data on the anxiety disorders. There is remarkably sparce literature on the prevalence, risk profile, diagnosis, natural course, and treatment response of anxiety disorders in children, adolescents, and old age. Neuroimaging studies of late-life anxiety disorders are virtually nonexistent. Although the magnitude of this deficit alone is impressive, when considered in the context of the rapidly growing geriatric population, the lack of anxiety disorder studies in the elderly is stunning.

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The pharmacopoeia of available medications for the treatment of anxiety disorders is large and varied, but significant shortcomings persist. Rapid symptom relief, which is important to many patients with anxiety disorders, has remained an elusive goal for all treatments save the benzodiazepines. In addition, remission has become the new gold standard of treatment efficacy in psychiatry, but few of the existing antidepressants or anxiolytics have been put to the test of achieving full recovery. We should no longer accept the modest and incomplete therapeutic responses attained by so many of our patients. An emerging literature suggests that the addition of a second drug with a different mechanism of action is one method to improve clinical outcome to monotherapy. The efficacy of the atypical antipsychotics as augmentation therapy for refractory anxiety disorders is suggested by a small, but growing, number of controlled trials. Ideally, an atypical antipsychotic for use as augmentation therapy would convert nonresponders to responders and would be associated with a low rate of adverse effects, such as benzodiazepine-related abuse/dependence liabilities, weight gain, excessive sedation, and untoward effects on glucose metabolism and serum lipids. Aripiprazole is a next generation antipsychotic with a novel mechanism of action and an impressive safety and tolerability profile that has been shown to improve anxiety symptoms in patients with schizophrenia. Further studies of novel therapeutic approaches are warranted to increase rates of response and remission to anxiety disorder treatment and improve clinical outcome.