Understanding Posttraumatic Stress Disorder: From Diagnosis and Neurobiology to Treatment
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Guest Editor

this issue of *Psychiatric Annals* focuses on posttraumatic stress disorder (PTSD), a severe psychiatric disorder that is increasing in prevalence. Compared to other psychiatric disorders, such as major depressive disorder and bipolar disorder, PTSD is poorly understood both in terms of pathophysiology and choice of appropriate treatment. Consequently, many patients continue to suffer with the devastating symptoms of PTSD. The contributors for this issue are leaders in the psychiatry field, and they contribute articles that provide in-depth insight into diagnosis and neurobiology, as well as therapeutic options for PTSD.

Dr. Eric Vermetten and colleagues discuss the major controversies concerning the nosology of PTSD with an emphasis on the changes in the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (*DSM-5*) and *ICD-11*. In spite of the increasing data supporting a biological basis for disease vulnerability and the repeated brain alterations demonstrated in PTSD patients, there remains those who continue to claim that PTSD is not a validated psychiatric diagnosis. What is undeniable is the fact that up to 30% to 40% of people exposed to severe trauma develop a set of disabling symptoms including avoidance, re-experiencing the trauma, and numbing as well as mood disturbances and cognitive impairment that markedly alter social and occupational functioning. The high rate of comorbid major depression and other Axis I disorders is not fundamentally different than other conditions documented in *DSM-5* such as obsessive-compulsive disorder and in no way invalidates the PTSD diagnosis.

Drs. Julius C. Pape and Elisabeth B. Binder provide a comprehensive view of the state-of-the-art genetic and epigenetic contributions for the development of PTSD. Early twin and family studies revealed an important role for genetics in the diathesis for PTSD and more recent studies of gene X environment interactions have provided much needed novel information that has led to a better molecular understanding of how these interactions, mediated by epigenetic mechanisms, regulate gene transcription. A number of candidate genes, particularly those, not surprisingly, associated with the hypothalamic-pituitary-adrenal axis, appear to play a major role in regulating risk for PTSD after trauma exposure. These include polymorphisms of the corticotropin-releasing hormone type 1 receptor, glucocorticoid receptor, NCR3R1 and FKBP5, a glucocorticoid receptor co-chaperone protein, as well as the pituitary adenylate cyclase-activating polypeptide receptor 1, and the opioid-receptor-like 1. Although genome-wide association studies (GWAS) have proven to be a useful strategy to uncover common genetic variations associated with various other medical and psychiatric disorders, the relatively small sample size of the early studies has hampered progress. The newly formed PTSD GWAS consortium
may rectify these problems and provide novel findings, although neither the much larger major depression nor schizophrenia GWAS have, arguably, resulted in startling new findings. The emerging role of epigenetic mechanisms in concert with specific genetic polymorphisms (eg, FKBP5) in PTSD vulnerability is described, as is the burgeoning field of noncoding ribonucleic acid (RNAs), including microRNAs.

Drs. Daniel W. Grupe and Aaron S. Heller critically review the structural and functional brain imaging findings in PTSD. They make the extraordinarily important point of the need to distinguish between the neural consequences of trauma and the neurobiology of PTSD, a variable not well-controlled in most studies. Taken together, the extant literature does indicate alterations in the medial prefrontal cortex-amygdala-hippocampal circuitry in PTSD. They highlight a substantial number of deficiencies in the current database, most notably the importance of trauma subtype, the age at the time of trauma, the magnitude and chronicity of the trauma, and the interactive effects of early life trauma and adult trauma.

Drs. Erika J. Wolf and Paula P. Schnurr focus on a too long-ignored area—the relationship of PTSD and cardiometabolic health. It is now clear, according to their article, that PTSD is associated with an increased risk for metabolic syndrome and coronary artery disease, including myocardial infarction and stroke. They provide evidence that this relationship is mediated, in part, by accelerated cellular aging facilitated by epigenetic mechanisms.

Finally, Dr. Nils C. Westfall and I review PTSD treatment modalities in literature. There is general and widespread agreement that trauma-focused psychotherapies including exposure therapy and cognitive-processing therapy are evidence-based efficacious first-line treatments. Eye movement desensitization and reprocessing has some low-strength evidence for efficacy. There is insufficient evidence to recommend psychodynamic psychotherapy for PTSD. There are some limited data suggesting the utility of interpersonal psychotherapy and mindfulness-based therapy as well as hypnotherapy for PTSD. In terms of pharmacotherapy, both sertraline and paroxetine are US Food and Drug Administration-approved for the treatment of PTSD, and there is evidence for the efficacy of venlafaxine. Antipsychotic drug augmentation of antidepressants in PTSD does not appear to be effective. Prazosin clearly is effective in reducing PTSD-associated nightmares. Unfortunately, neither psychotherapy nor pharmacotherapy nor their combination frequently result in remission of symptoms in patients with PTSD (see the Westfall and Nemeroff article, this issue).

Clearly, a better understanding of the pathophysiology of PTSD will be necessary before novel and more effective treatments can be developed.

REFERENCES

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He has received a number of research and education awards including the Kempf Award in Psychobiology, the Samuel Hibbs Award, Research Mentoring Award, Judson Marmor Award, the Vestermark Award from the American Psychiatric Association (APA), the Mood Disorders Award, Bowis Award, and Dean Award from the ACP. He was elected to the Institute of Medicine of the National Academy of Sciences in 2002.

His research has focused on the pathophysiology of mood and anxiety disorders with a focus on the role of child abuse and neglect as a major risk factor. He has also focused on the role of mood disorders as a risk factor for major medical disorders including heart disease, diabetes, and cancer. He has served on the Mental Health Advisory Council of the National Institute of Mental Health and the Biomedical Research Council for NASA. He is the co-editor-in-chief of the Textbook of Psychopharmacology, published by the APA. His research is currently supported by grants from the National Institutes of Health.

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