Special Section on Sexual Dimorphism in Neuroimmune Cells — Commentary

Sexual Dimorphism of Neuroimmune Cells and Its Impact on the Central Nervous System: a Special Issue

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ABSTRACT

Neuroimmune-related sex differences contribute to the complexity of neurologic disorders, such as drug abuse, depression, and chronic pain. The collection of articles presented in this issue add to our understanding of sex as a critical biologic variable in the study of psychiatric and neurologic diseases.

SIGNIFICANCE STATEMENT

Consideration of sex in the design and interpretation of study results is critical. Sex differences may warrant different treatment approaches for diseases in which sex or gender influences disease outcomes. The studies and reviews presented here examine the contribution of sexual dimorphism in the physiologic responses and pharmacological treatments of neurological and psychiatric disorders.

Sex-dependent differences in neuroimmune cells have recently been recognized as a differentiating factor in physiologic settings, including synapse remodeling and maturation and postnatal development. These differences have implications for gender-specific brain wiring and for the treatment of neurologic and psychiatric diseases. This special issue of the journal showcases original research and reviews pertaining to the broad and intricate repertoire of neuroimmune-related sex differences and their impact on the central nervous system. Two American Society for Pharmacology and Experimental Therapeutics symposia during the Experimental Biology conference in April 2019 focused on the biologic manifestations of such differences. Presenters in the two symposia, one of them hosted by the authors of this introduction, provided the content included here.

The cells involved in immunoregulation of the central nervous system are an exciting line of research and a potential therapeutic target for neurologic diseases. We start this issue with a review by Gopinath et al. (2020) outlining the roles of peripheral myeloid and neuroimmune cells in the healthy brain as well as their compromised contributions in the context of Alzheimer and Parkinson disease. Gustavo Martinez-Muniz and Susan K. Wood (2020) summarize recent preclinical and clinical studies that examine how stress induces inflammation and how inflammation may lead to depression. They also describe the sex differences in the immune response to stress, the role of antidepressant therapy on inflammation, and the antidepressant-like effects of anti-inflammatory compounds. Alexandros G. Kokkosis and S.E. Tsirka (2020) present recent evidence on the aberrant activation of neuroimmune cells and their impact on mental health disorders as a whole. They examine the role of sex hormones, genetics, and environmental factors on the etiology of neuropsychiatric conditions. Following up on distinct neuropsychiatric susceptibilities, Paul W. Czoty and Michael A. Nader (2020) showcase their work on lofexidine and guanfacine, two α-2 adrenergic receptor agonists that have modest effects on reducing cocaine choice in male and female cynomolgus monkeys.

Halievski et al. (2020) review past literature on sex-dependent differences in microglial P2X4R signaling, emphasizing how these differences might hinder proper treatment of chronic pain in both males and females.

Ewald et al. (2020) give us insight into the role of microglia in the modulation of the neuronal circuits that control breathing. Their work shows major transcriptomic differences in various microglial populations depending on their central nervous system location as well as significant sex-dependent differences in gene expression in spinal cord microglia. Their findings may shed light on the cellular mechanisms responsible for the anatomic differences in breathing control seen in males and females.

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These articles point to our new understanding that neuroimmune-related sex differences play an important role...
in the physiologic and pharmacological responses to neurologic disorders. As additional reports become published describing such differences, it becomes increasingly evident that sex as a biologic variable is indeed critical and should be taken into account in the design and interpretation of study results. Such design may be even more complex when gender differences become accounted for as well. We hope to have provided an initial collection of important work being done in this area and to have shown how advances in this field might shape treatments for neurologic and psychiatric disorders in the future.

References


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