Toward a Better Understanding of the Relationship Between Vulvodynia and Chronic Stressors

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AS CLINICIANS WHO devote a significant amount of their professional time to the study of vulvodynia and to the care of women with this chronic pain condition, we applaud the work of Khandker and colleagues, who provide data on the important role that stress appears to have in women with this condition. Although more and more data are emerging that not only confirm the genetic predisposition to wellness and disease in each of us, of note, there are also a large number of studies, including this one by Khandker and colleagues,¹ that confirm the role of epigenetics.

As early as 1936, Hans Selye famously observed that “every stress leaves an indelible scar” in characterizing the first modern series of stress studies which he entitled the General Adaptation Syndrome.² More recently, animal models have been begun to clarify the centrally based mechanism of stress—pain development.³ The pivotal role of biopsychosocial stressor and their interplay is emerging as important in relation to chronic pain disorders, such as vulvodynia (the condition presented in this journal issue), interstitial cystitis, temporomandibular joint disorder, and fibromyalgia, to the central sensitivity syndromes such as irritable bowel syndrome, chronic fatigue syndrome, and posttraumatic stress syndrome and to mood disorders. In addition, the biopsychosocial interplay in humans is also being noted in conditions far removed from pain and affective syndromes, such as weight gain tendencies and weight loss success. From the perspective of early childhood maltreatment or neglect, these differences are not unexpected. Cortical thickness measures of the brain appear to show marked differences between those who did and those who did not experience extreme childhood stressors.⁴ The impact of these adverse changes is being studied and most likely is contributing to and influencing pain neuronal circuits.

Now having objective data that point to the importance of chronic stressors confirms what most clinicians have subjectively noted in their clinical practice when dealing with vulvodynia patients: that many have this history. Teasing out the other contributors to vulvodynia is also a research imperative. What role does genetics, the female sex, early in-utero exposures, sexual versus physical versus emotional abuse, trauma, chronic infection, abnormal nociceptive pro-

cessing, accompanying connective tissue disorders, deconditioning autonomic dysregulation, etc.—even the role of geographic area with various climates, toxins, and pollutants—play in the final outcome of having chronic vulvar pain?

In our NIH clinical trial we are measuring biological correlates of response to better characterize vulvodynia and defining which women respond to treatment, including assessment of central versus peripheral sensitization, pelvic hypertonicity, tender point tenderness, and autonomic dysregulation. These measures were selected based on research suggesting that the underlying pathophysiology of vulvodynia may be related to abnormalities in the central nervous system pain pathways, pelvic floor muscles, or the vulvovaginal epithelium, many of which may have a stress initiator or contributor. Characterization of these women by various measures will add to our depth of knowledge regarding etiology of this chronic pain condition.

Specifically, we are using the capsaicin skin sensitivity test to measure central sensitization in conjunction with measurement of heart rate variability to assess autonomic dysregulation.^{5,6} An algometer, a mechanical pulse generator, is being applied to the vulvovaginal epithelium to serve as a precise measure of peripheral sensitization.⁷ The tender point tenderness examination and a vaginal algometer, a device developed to standardize digital examination of the pelvic floor, are being used to measure muscular correlates of response.⁸ These data in the paper by Khandker and colleagues will enrich our study results and hopefully add to the role of central nervous system contributors.

Clearly, basic and translational researchers are continuing to delve into the last front—our brain. One day the thousands of brain cells that communicate by electrical, chemical, and neural signals in response to every thought and behavior will be understood. It is already known that connections between brain cells change over time in response to the environment, and it follows that any etiology of chronic stress will affect who we are and how we feel from a health perspective. With the next generation of neural network models, the so-called spiking neural networks, we will not only understand the end result of brain modeling as it pertains to how people clinically

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present, as Khandker and colleagues' paper describes,¹ but will also be able to replicate brain activities in simulations that will uncover the solution of how to rewire the brain that has been subject to chronic stressors in conditions such as vulvodynia to eliminate chronic pain.

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Disclosure Statement

Dr. Bachmann served on an advisory board for TEVA Pharmaceutical Industries Ltd., which produces Neurontin, a generic equivalent to the study drug Gabapentin.

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