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Editorial

Sex and Psychiatry in the Next 5 Years

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The Institute of Medicine (IOM) report "Exploring the Biological Contributions to Human Health: Does Sex Matter?"[1] answers the question in its title with a resounding *sex matters at the cellular level*. The IOM report authors[1,2] used the term *sex* to designate genetic and biological phenomena linked to having the XX or XY chromosomal complement. The reproductive hormonal milieu is an example of the distinction between males and females; however, the effects of sex extend well beyond the reproductive system. Research has revealed the obvious but often ignored fact that women are not small men from a physiologic perspective. For example, distinct sex-based regional differences in fatty acid mobilization, oxidation, and storage occur. Women store fat in the gluteal and femoral regions, while men store fat in the abdominal area.[3] Basal fat oxidation is lower in females compared with males, which contributes to higher fat storage in women. Men are at greater risk for cardiovascular and renal disease than are age-matched, premenopausal women.[4] Blood pressure is higher in men than in women at similar ages; however, after menopause, blood pressure increases in women to levels higher than in men. Boys suffer from asthma more frequently than girls until puberty, when the sex ratio reverses.[5] Testosterone has immunosuppressant properties, while female sex steroids are pro-inflammatory. If the virilization of steroids can be averted, therapy is a possibility.[5] For example, the weakly androgenic adrenal steroid dehydroepiandrosterone decreased disease activity in women with systemic lupus erythematosus, and concurrent prednisone doses were reduced.[6]

Gender is the term used to refer to the psychosocial expression of living as a man or a woman.[1,2] *Gender* is a proxy term for a highly complex set of biological, psychological, and behavioral processes. The occurrence of two genders is a great experiment of Nature and an opportunity to understand variability in disease expression.[7] We observe gender effects in our work daily. In discussing a patient with eating disorder, why can we make a reasonably accurate assumption that the person is female? Why are antipsychotic drug doses to which women respond typically lower than for men? If we ask these questions, we can develop hypotheses about factors associated with disease states that can be tested.

The IOM identified a number of gender-specific concepts that are critical to health.[1,2] The risk for disease is the result of genetically related vulnerabilities that interact with a complex set of environmental exposures. As psychiatrists, we are medical specialists who are uniquely positioned to explore the gender-specific biological and behavioral effects of these exposures. For example, females suffer sexual victimization, an exposure associated with risk for numerous mental illnesses, more frequently than males.[8] Gender is the single strongest correlate of risk for many different mental disorders in epidemiologic research.[7] The increased risk in females of major depressive disorder emerges at Tanner stage III of sexual development.[9] Because Tanner stage has a much larger impact than age or menarche on the emergence of depression, the interaction of Tanner stage–specific physiologic change with environmental factors is important to the phenomenology of risk elevation. In prepubertal males, developmental disorders are much more common than in females.[10] Why are these disorders distributed differentially by gender in the human population?

A major mandate of the IOM reports is to apply a powerful analytical tool, the gender-focused analysis, to all

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health research. The potential of this tool reaches beyond women's health to the establishment of comparative disease risks for women and men. Both genders will benefit. Every aspect of disease phenomenology in a population (environmental toxic exposures, vulnerability to disorder, symptomatology, style of symptom expression, natural history, treatment choice, treatment responsivity, social support, and functional capacity) is affected by gender.[7] In the Research Agenda for DSM-V,[11] the incorporation of gender and culture concepts into all domains of psychiatric research was recommended. At the inception of every research project, we must ask how knowledge about the study question can be maximized through incorporation of gender considerations. Capturing variables related to disease expression is precisely the process that comprises the rich opportunity for hypothesis generation, testing, and new knowledge in psychiatry. The benefits of gender-specific analyses provide immense potential for improved conceptual models and therapies across the whole of our field.

Developers of the NIH Roadmap (http://www.nihroadmap.nih.gov) observed that "increasingly, scientific advances are being made at the interfaces of traditional disciplines, and that approaches to science are becoming more integrative." They encouraged investigators from diverse backgrounds to work across traditional disciplinary boundaries to answer scientific questions. Let me dream of the possibilities! Before the close of this decade, we will make good neighbors of physicians who usually work in different specialty pigeonholes. We will partner with pediatricians and gynecologists to screen girls for the emergence of psychiatric episodes at puberty. Identification, education, and treatment will prevent the derailment of psychosocial development by averting episodes. Young women will be prepared to self-monitor and manage depressive recurrences through disease management programs. To achieve optimal therapeutic response, we will prescribe gender-specific multimodal treatment plans for patients with schizophrenia.[12] We will provide female patients with lower doses of antipsychotic drugs and family therapy intervention, from which they benefit while male patients do not. Males will have aggressive drug regimens, treatments to reduce interpersonal aggression and addiction, and behavioral programs to achieve successful integration into structured long-term settings. These different treatment approaches were derived directly from observed gender differences in schizophrenia research.[12]

"Health care organizations tend to view the need for gender-based medical approaches as merely a customer service issue rather than a reorientation in medical practice."[13(p81)] This powerful statement captures the challenge. Emboldened by Surgeon General David Satcher's report,[14] we proclaim that mental health is fundamental to health. We are medicine's biobehavioral experts. Let us lead the march to reap the rich yield from gender-specific research across the next 5 years.

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