Introduction

The Dynamics of Sex: Gender Differences in Psychiatric Disorders

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In recent years, the increasing attention that has been paid to gender as an important variable in the expression and treatment of psychiatric disorders has resulted in a number of important findings. These new observations are well represented in this special issue, "The Dynamics of Sex: Gender Differences in Psychiatric Disorders."

Overall, mood and anxiety disorders are both more common in women than in men.[1,2] More specifically, panic, phobias, and obsessive-compulsive disorder are all more common in women than in men,[1] as is major depression and dysthymia.[1] In spite of these clear differences in prevalence, we have had relatively few data on the possible biological explanations for such differences. Moreover, there has been a paucity of information on how gender affects response to treatment, side effects, and so on. Fortunately, this state of affairs is rapidly changing.

There are a number of historical reasons for our lack of data in these areas, and these have been reviewed nicely elsewhere.[3] Generally, animal models/paradigms used to study psychiatric disorders or pharmacologic effects have relied on males, in part because of the confusing effects of the estrous cycle on brain neurochemical activity. This has resulted in our not knowing how a background of female reproductive hormones might alter drug effects.

The thalidomide experience a few decades ago caused great concern in this country and an even further tightening of the constraints on exposing women of childbearing potential to the possible harmful fetal effects of investigational agents. Women were effectively excluded from phase 1 and 2 trials of new agents, leaving a gap in our understanding of how younger women may be affected by these drugs. This conservative approach was carried over into phase 3 trials as well. Thus for many years, new psychotropic agents have commonly been released with little knowledge about their effectiveness or tolerability in younger women, their potential interactions with exogenous hormones, or their effects on the fetus. This state of affairs had generally not been taken seriously enough by the medical establishment, which frequently assumed that various agents would be equally effective, well tolerated, and safe in both men and women. Unfortunately, some recent data from Halbreich and colleagues suggest that women psychiatric patients may be at increased risk for breast cancer, perhaps reflecting the effects of antipsychotics on prolactin production and excretion.[4]

In the past few years, the tide has begun to change, largely through the political process. Women have demanded more pre-release knowledge about how drugs will affect them. A number of important initiatives have supported this change in our approach to studying new pharmacologic agents in women.

First, the U.S. Public Health Service (PHS) released a task force report on women's health issues in 1985.[5] This report provided a framework for reassessing the status of key health issues as they related to women. In 1991, two events also proved of vital importance in rectifying the situation. The American Medical Association (AMA) Council on Ethical and Judicial Affairs published its position paper, "Gender Disparities in Clinical Decision

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Making," in the *Journal of the American Medical Association* (JAMA).[6] That same year, the PHS released its Action Plan in Women's Health. This was followed by the passing of the Women's Health Equity Act in 1993 and the appointment of the First Deputy Assistant Secretary for Women's Health in 1994.

The Women's Health Equity Act called for a number of initiatives in both research and services for women. Regarding research, it required that the National Institutes of Health (NIH) establish guidelines for including women and minorities in clinical research. Drug companies were required to include women in clinical trials, examine gender differences in phase 3 trials, and study the interaction of new drugs with gonadal hormones prior to Food and Drug Administration (FDA) approval. It also expanded National Institute for Alcoholism and Alcohol Abuse research on women and alcoholism and NIH research on AIDS in women.

Regarding services, the act established offices of women's health at various federal agencies (e.g., FDA); information programs on prevention and treatment of eating disorders at Center for Mental Health Services; and women's health services and research programs at the Veterans Administration. It also required the PHS to study adding women's health courses to health professional school curricula. All of these initiatives are beginning to have an impact on our knowledge of women's health.

This special issue contains five papers on gender and psychiatric disorders. The emphasis is on women because of the emerging wave of new data in this area. Ellen Leibenluft, M.D., discusses issues in the treatment of women with bipolar illness, with emphasis on the increased risk of rapid cycling bipolar disorder in women. Susan G. Kornstein, M.D., reviews gender differences in the presentation and treatment of major depression. The paper by Alexis M. Llewellyn and colleagues reviews depression during pregnancy and the postpartum period. Carol A. Tamminga, M.D., reviews important differences between men and women in onset and course of schizophrenia. Lastly, Kimberly A. Yonkers, M.D., discusses premenstrual dysphoria and optimal treatment strategies.

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