Gender Differences in Psychiatry
Epidemiology and Drug Response

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Summary

There are important gender differences in the epidemiology of psychiatric disorders and in the effects of drugs used to treat these disorders. Women are major consumers of psychotropic drugs, but they have often been excluded from drug trials that establish tolerability and dose parameters. Because women have a higher proportion of adipose tissue than men, higher plasma drug concentrations and longer elimination half-lives can occur in women.

In this review, gender differences are examined for the most prevalent diagnoses with a tradition of pharmacological responsivity. Anxiety disorders are generally more common in women, although social phobia and post-traumatic
stress disorder may have an equal gender distribution. Obsessive-compulsive disorder has a slight preponderance in women, while patients with generalised anxiety disorder and panic disorder are predominantly women. Benzodiazepines that undergo conjugation appear to have a longer elimination time in women, and concomitant administration of oral contraceptives can decrease clearance of these drugs.

Women are twice as likely to have a major depression and equally likely to have bipolar disorder as men. However, women are overrepresented in the rapid cycling variant of bipolar disorder. Gender data on antidepressant response are mixed, but women are more vulnerable to lithium-induced hypothyroidism. Men and women have equal risk for schizophrenia, but vary in terms of clinical features such as premorbid functioning, age of onset and outcome. Women tend to require lower dosages of antipsychotics, experience a greater improvement in symptoms when receiving these drugs, but are at a higher risk of developing tardive dyskinesia. The incidence of eating disorders (anorexia nervosa and bulimia nervosa) is higher in females than in males.

Future attention to gender differences will improve the diagnosis of, allow for more accurate prognosis of, and promote individually designed interventions for psychiatric disorders.

Only recently has increased attention been paid to gender differences in pharmacokinetics and pharmacodynamics. In the US, it has taken a federal mandate to increase diversity in drug trials by legislating for the inclusion of women and different ethnic groups. Although women use more prescription drugs and experience more adverse effects than men, much of the research to establish tolerability and dose parameters has involved only young men. Because of past adverse outcomes (such as fetal deformities associated with thalidomide, and diethylstilbestrol-associated vaginal neo­plasia), there has been a generalised hesitancy to use young women in drug research. Other researchers exclude women because of hormonal fluctuations, or fail to examine possible menstrual cycle effects. Many studies that examine gender differences appear to do so incidentally. Yet, there are clear gender differences that could affect drug response.

The proportions of muscular and adipose tissue influence a number of pharmacokinetic parameters including volume of distribution and elimination half-life. Due to a higher proportion of adipose tissue, women are likely to have a higher volume of distribution and lower serum drug concentration in proportion to dosage. However, over time, women may have an increased risk for accumulation of drugs in adipose tissue, with a resulting lengthening of half-life and increase in plasma concentrations. In addition to gender differences in menses and drug distribution, there may also be gender differences in absorption, bioavailability and metabolism. It has been demonstrated that premenopausal women have a shorter gastrointestinal transit time during the follicular phase, while others have suggested that estrogen and progesterone may have an inhibitory effect on gastric emptying. The use of oral contraceptives may inhibit or promote hepatic metabolism of concomitantly administered drugs.

The gender of the patient can convey some diagnostic and prognostic information. Psychiatry has long recognised gender differences in the prevalence and gender ratio of disorders. Whenever they have been available, these data have been included in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). DSM-IV has been refined in this area by studies such as the National Institute of Mental