Chapter

18

Anxiety disorders in women

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Anxiety is a common human experience, and varies in depth and intensity. The experience most typically occurs in response to life stressors and may be temporary. However, many people experience anxiety symptoms that comprise a diagnosable mental illness. Individuals with an anxiety disorder are functionally impaired by the condition that is beyond a reasonable temporary response to trauma, stress or danger.

Anxiety disorders are highly prevalent and persist, frequently with periods of remission and relapse across the life-course (Yonkers, 2003). They are universally reported to be more common in women than men. For example, Australian data from the Australian Survey of Mental Health and Wellbeing, conducted in 2007, estimated the weighted 12-month prevalence of any anxiety disorder, diagnosable using DSM-IV criteria, as 14.6% for women and 8.9% for men (McEvoy et al., 2011).

The US National Comorbidity Survey (NCS), a community prevalence study, found the following risk factors to be associated with a lifetime anxiety disorder: lower income, less education, living in the northeast and female sex. The likelihood of developing an anxiety disorder was 85% higher in women than men. In a prospective, longitudinal, population-based study of 643 women, psychosocial variables were examined to evaluate whether it was possible to predict the onset of a new anxiety disorder or the recurrence of an existing disorder. The presence of anxiety disorders was assessed every 6 months over a 3-year period, using the Structured Clinical Interview for the Diagnostic Statistical Manual for Mental Disorders (SCID) and significant predictors of anxiety were found to include a history of anxiety, increased anxiety sensitivity (meaning the fear of anxiety-related sensations) and increased neuroticism (Calkins et al., 2009). The

prevalence over 12 months of specific types of anxiety disorders in women (Kessler et al., 2012) were recorded as follows: specific phobia 12.1%, social phobia 7.4%, post-traumatic stress disorder 3.7%, generalized anxiety disorder 2.0%, separation anxiety disorder 1.2%, panic disorder 2.4%, agoraphobia 1.7%, and obsessive-compulsive disorder 1.2%.

Anxiety disorders often exist comorbidly with major depressive disorder and the lifetime prevalence in a sample of (n=1970) Chinese patients surveyed to assess the association between major depressive disorder and comorbid anxiety disorders found the lifetime prevalence rate for any type of comorbid anxiety disorder was 60%, which is consistent with findings from European and American studies (Li et al., 2012).

The degree of disability women experience as a result of anxiety disorders was explored by McLean and colleagues (2011) in a pooled data set of 20,000 adults from the Collaborative Psychiatric Epidemiology Studies (CPES). Women had higher rates of a lifetime diagnosis for each of the anxiety disorders (aside from social anxiety disorder) and were more likely to be diagnosed with more than one anxiety disorder. Anxiety disorders were associated with a greater illness burden in women than men.

The gender difference in the prevalence of anxiety symptoms is evident even during childhood (Hayward et al., 2000; Lewinsohn et al., 1998; Wittchen et al., 1998). Boys and girls begin to experience the onset of pathological anxiety at about the same age (Lewinsohn et al., 1998; Wittchen et al., 1998) but girls are more vulnerable.

In this chapter, we review sex differences in the epidemiology, clinical characteristics and illness course for the anxiety disorders, excluding post-traumatic stress disorder (this is the focus of Chapter 17 in this

book). Additionally, we discuss the influence of the premenstruum as well as gestation and delivery on the expression of anxiety disorders, but treatment of anxiety disorders is not addressed in this chapter.

Generalized anxiety disorder

Generalized anxiety disorder (GAD) is defined as excessive worry about a number of events or issues that is difficult to control. Worry is experienced for at least 6 months and may be accompanied by restlessness, fatigue, difficulty concentrating, irritability, muscle tension and sleep disturbance. The worry cannot be limited to a core feature of another syndrome, for example, worry about having a panic attack or gaining weight because in that case, it would be supportive of the other condition and not GAD.

In the Epidemiological Catchment Area Study (ECA), the prevalence of GAD was determined using DSM-III criteria, which stipulates only 1, rather than 6 months of illness (DSM-III-R and DSM-IV) (Blazer et al., 1991). The 12-month prevalence rate in women was about twice as high as it was for men (2.4% in men and 5.0% in women). Those at greatest risk were African-American women under 30 and Hispanic women aged 45–64; the rates in both of these groups was greater than the rate in Caucasian women (Blazer et al., 1991).

According to the NCS, 3.6% (se=0.5) of men and 6.6% (se=0.5) of women will meet criteria for DSM-III R GAD at some point in their lives (Wittchen et al., 1994). In that dataset, women were 63% more likely to develop GAD than were men (Wittchen et al., 1994).

Women with generalized anxiety disorder report intrusive, pervasive worries that affect their function and quality of life across many domains (Grant et al., 2005). The majority of people with generalized anxiety disorder are diagnosed and managed within primary care, with many people initially presenting with physical symptoms, rather than the psychological symptoms. Physical symptoms can include fatigue, muscle tension, palpitations, and a sensation of constricted breathing or be associated with a tremor or sleep disturbance. These physical symptoms can cause significant distress and functional impairment.

Generalized anxiety disorder usually has an onset prior to 25 years of age and most often has a chronic course (Stein et al., 2005). In a US study, generalized anxiety disorder was second only to substance abuse in terms of population prevalence (Fricchione et al.,

2004). Individuals with generalized anxiety disorder have a significantly increased risk of developing subsequent depression (Hettema et al., 2006) with up to 75% of sufferers developing a major depressive episode in their lifetime. Individuals with comorbid generalized anxiety disorder and depression are more disabled than those with either disorder alone (Grant et al., 2005).

Risk factors for the development of generalized anxiety disorder include a family history of generalized anxiety disorder, as well as stress and trauma. A neurobiological model of generalized anxiety disorder suggests that the early life experience of elevations of adrenaline and cortisol, as a result of exposure to stressful situations, may upregulate and hypersensitize the HPA axis in adulthood (see also Chapter 17). The possible transgenerational transmission of generalized anxiety disorder is worth considering in this context given that the infants of women with anxiety disorders in pregnancy are more likely to be exposed to greater circulating levels of adrenaline in-utero, meaning that they are more vulnerable to developing anxiety disorders in childhood if exposed to early life trauma. Social stressors may have a divergent impact on the risk of depression and anxiety in men and women (Cameron & Hill, 1989). In a 3-year longitudinal study of English women, danger predicted later anxiety, while loss predicted depression (Brown et al., 1996); a combination of loss and danger led to comorbid anxiety and depression. External support did not modify the effect of these events.

Clinical course

Generalized anxiety disorder has a generally chronic course throughout the lifetime for both women and men (Pigott, 1999) although comorbidity decreases the chance of recovery particularly if there are comorbid personality disorders from either cluster B or cluster C (Yonkers et al., 2000). The majority of adults with GAD experience the illness for over 5 years (Blazer et al., 1991), and women and men have approximately the same likelihood of experiencing a remission (probability 0.46 in women and 0.56 in men; Log rank χ^2 = 1.39 (df=1); p=0.24) (Yonkers et al., 2003).

Comorbidity

GAD is most often comorbid with other conditions, with the US National Comorbidity Survey

discovering that over 90% of people diagnosed with GAD had a comorbid diagnosis, including dysthymia, depression, somatization, other anxiety disorders, bipolar disorder or substance abuse. In their longitudinal study, Yonkers et al. (1996) found that 23% of GAD subjects had two, and 16% had three or more other anxiety disorders active at initial assessment. GAD can also occur comorbidly with eating disorders; a systematic review, considering two observational studies (*n*=55), found a lifetime prevalence of GAD among people with anorexia nervosa of between 24% and 31% (Dyck et al., 2001).

Comorbidity of depression and GAD is particularly common (Angst & Vollrath, 1991). Some research suggests shared inheritance of these disorders (Kendler et al., 1992). Both women and men who have anxiety coupled with depression have a poorer outcome (Angst & Vollrath, 1991; Durham et al., 1997). There is also evidence that a history of GAD predisposes individuals to develop major depression (Parker et al., 1997), although this effect may not be limited to GAD amongst the anxiety disorders (Breslau et al., 1995). Another possibility is that an anxiety disorder increases the risk for a mood disorder and vice-versa (Hayward et al., 2000; Kessler et al., 2003).

Comorbidity between anxiety disorders and alcohol abuse and dependence disorders is also very common (Massion et al., 1993; Yonkers et al., 1996). Anxious symptoms may increase the susceptibility to alcohol consumption (Fischer & JW, 1998). Men are overall more likely to abuse drugs and alcohol, but moderate anxiety in depressed women seems to increase their risk for alcohol abuse (Fischer & JW, 1998). Other work has found an association between alcoholism and anxiety disorders that is greater for phobias than for panic or generalized anxiety (Merikangas et al., 1998).

Some authors propose that the expression of anxiety in depressed women may differ from anxiety in depressed men (Katz et al., 1993; Parker et al., 1997). For example, highly anxious depressed women may express their anxious-depressive symptoms through motor retardation and vagueness, with less evident body movement, while men may show hostility and increased visible body agitation (Katz et al., 1993).

Panic disorder

Panic disorder is a pattern of brief but intense, recurrent and usually unanticipated episodes of fear or discomfort that occur without a notable precipitant. In DSM-5, panic disorder remains classified as an anxiety disorder and the diagnostic criteria specify that episodes of panic must be present for over 1 month and that an individual must experience a continual fear of having future attacks and display avoidance of certain situations in an attempt to prevent further attacks.

A change in DSM-5, in comparison to DSM-IV, is that panic disorder was previously classified as occurring with, or without, agoraphobia, while in DSM-5, agoraphobia is listed as a separate condition. In practice though, co-occurring panic disorder and agoraphobia will remain prevalent given that panic disorder leads to functional impairment in patients predominantly through the limitations on their lifestyle engendered by fear of future panic attacks.

The physical symptoms associated with panic attacks are driven by overactivation of the sympathetic nervous system and include palpitations, sweating, feeling short of breath or a choking sensation, nausea or abdominal discomfort, feeling dizzy, having a sense of unreality, numbness or tingling, chills or hot flushes, and a fear of dying or losing control (APA, 1994). The cognitive features may include acute fear of dying, losing control, going mad and a need to escape from the current situation, and there can also be a feeling of depersonalisation or derealization.

Estimates suggest 1–2% of the adult population suffer panic disorder (Yates, 2009). Common risk factors for the development of panic disorder include female gender, low socioeconomic status and anxious childhood temperament. Panic disorder is associated with an elevated risk of suicide as well as all-cause mortality and cardiovascular disease. It ranks highest among the anxiety disorders in terms of disease burden.

Women and men with panic disorder tend to experience their symptoms somewhat differently. Data from the NCS show that, compared to men, women were more likely to endorse shortness of breath, nausea and a perception of being smothered; men were more likely to identify difficulties with sweating and stomach pain (Sheikh et al., 2002). The greater proclivity for women to develop respiratory symptoms is interesting in light of results from provocation studies. Women with panic may have greater sensitivity to panic-inducing respiratory challenge than their male counterparts (Papp et al., 1997; Papp & Gorman, 1988; Sheikh et al., 2002). Work by one group found that women have a higher resting

breathing rate and lower end-tidal CO_2 that may increase anxiety sensitivity (Papp et al., 1997; Papp & Gorman, 1988).

There has been interest in the conceptualization of anxiety disorders as resulting from psychopathology during childhood, in particular in relation to the presence of separation anxiety disorder in childhood. A meta-analysis of 20 studies indicated that children with separation anxiety disorder were more likely to develop panic disorder in adulthood (odds ratio=3.45; 95% CI=2.37–5.03). Additionally, there were five studies which suggested that a childhood diagnosis of separation anxiety disorder increased the overall risk of the development of future anxiety disorders in adulthood (odds ratio=2.19; 95% CI=1.40–3.42) (Kossowsky et al., 2013).

There has been particular interest in the effectiveness of MAO inhibitors in the treatment of panic disorder given previous studies of MAO inhibitors in animal models of panic disorder (Reif et al., 2012). Recent research focused on the gene encoding monoamine oxidase A (MAOA) in women. A meta-analysis of four studies with a pooled sample size of (n=1,115 patients and n=1,260 controls) reported a significant female-specific association when calculating an allelic model in panic disorder, leading the authors to suggest that "this sex-specific effect might be explained by a gene-dose effect causing higher MAOA expression in females." Furthermore, they hypothesize that high-expression MAOA-uVNTR alleles significantly increase the risk of women developing panic disorder. This finding will require further replication in larger samples, but may be a lead in the appreciation of female vulnerability to the development of panic disorder (Reif et al., 2012).

In a prospective study 2,325 female twins were examined using structural modelling to determine how genes, childhood, past-year environmental stressors, personality and episodes of major depression and generalized anxiety disorder influence an etiological model for symptoms of anxiety and depression (Kendler et al., 2010). The model that fit the data best revealed two etiological pathways. The first, a "trait-like" pathway reflects personality vulnerabilities that were mediated by genetic and early environmental risk factors. The second was mediated through episodes of major depression, or generalized anxiety disorder, recent environmental adversities and "trait-like" factors that influence exposure to stressful events and increase the probability of the onset of a depressive or anxiety disorder. Chen et al. (2010) found that women with panic disorder who experienced panic attacks during pregnancy carry an increased risk of having small-for-gestational-age infants, and the adjusted odds ratio for having a preterm delivery was 2.54 (95% CI=1.09–5.93). It appeared from this study though that it was only if the symptoms were experienced during the pregnancy, and for those women with a historical diagnosis of panic disorder there were no adverse outcomes noted (Chen, Lin, & Lee, 2010).

Clinical course

In panic disorder, women and men have approximately equal rates of remission but women have a much greater likelihood of relapse of their condition. In a study evaluating the course of panic disorder, the relapse rate over 8 years of follow up was 3-fold higher in women compared to men (Yonkers et al., 2003). This relapsing course of illness in women may be caused by higher anxiety sensitivity, even after treatment is instituted and remission is attained. In some instances, this vulnerability may be mediated by biological differences in respiratory mechanics between men and women (Sheikh et al., 2002) or by the increased prevalence of comorbid psychiatric illness, such as depression, in women (Hayward et al., 2000).

Agoraphobia

Agoraphobia is the fear of being in a closed space or an area from which escape may be difficult. This typically leads to a modification of behavior in an attempt to avoid panic attacks. Bekker (1996) offers a thorough review of gender and agoraphobia, finding the illness more prevalent in women than in men, across both clinical and community samples. Specifically, data from the NCS found that when panic disorder is accompanied by agoraphobia, the 1-month prevalence rate for men is 0.4% (sd=0.2) while 1.0% (sd=0.3) of women meet criteria (Eaton et al., 1994). Agoraphobia without panic is somewhat more common and the lifetime prevalence rate in men is 3.5% (se=0.4) and in women is 7% (se=0.6) (Eaton et al., 1994).

In DSM-5, agoraphobia is now listed as a separate condition, a change from DSM-IV where it was listed as accompanying panic disorder in some individuals. The new diagnostic criteria for agoraphobia include

the experience of intense fear or anxiety in at least two agoraphobic situations, for example, using public transport, being outside the home alone, being in open spaces, being in public places (e.g., shopping centers), being in crowds or standing in a line with other people, or a combination of two or more of these scenarios. An essential part of the diagnosis of agoraphobia is that the individual also has to exhibit avoidance behavior that occurs due to the fear of experiencing a panic attack or anxiety-related symptoms in a situation where it would be difficult to escape or seek help. Overall, it is the avoidance behavior itself that most seriously affects the quality of life and functioning of people with agoraphobia as their world gradually reduces until, at its most severe, they are unable to leave the home.

Women tend to adapt to their agoraphobia by limiting excursions outside of the home, especially without a companion, significantly more than men (Bourdon et al., 1988; Starcevic et al., 1998). It is notable that this is often more culturally acceptable, in that women can work inside the home while men tend to work outside the home and thus are less likely to function adequately if they are homebound. There is also evidence to suggest women report a significantly greater reduction in quality of life as a result of their agoraphobia in comparison to men (Starcevic et al., 1998). This is consistent with other data showing that panic disorder with agoraphobia is a more severe condition in women than in men (Turgeon et al., 1998). Women expressed greater avoidance severity, more catastrophic fears and more frequent comorbidity of another anxiety disorder, most notably social phobia or post-traumatic stress disorder.

Comorbidity

Among a group of anxiety-disordered individuals presenting in a clinical setting, 72% of whom were female, there were no significant sex differences in psychiatric comorbidity (Apfeldorf et al., 2000). Other work has found that women are more likely than males to have a co-occurring anxiety disorder, namely social phobia or post-traumatic stress disorder (PTSD) (Turgeon et al., 1998). PTSD comorbidity did not predict higher agoraphobic avoidance.

Alcohol dependence is a significant comorbidity in agoraphobia and men with agoraphobia are more likely than their female counterparts to suffer from alcoholism (Bibb & Chambless, 1986; Starcevic et al.,

1998; Yonkers et al., 1998). Although this may reflect the overall higher rate of hazardous alcohol use in men compared to women (Kessler et al. 1994) some work finds a higher rate of alcohol abuse in male agoraphobics compared to male non-agoraphobics (Bibb & Chambless, 1986). In evaluating these sex differences, it is also important to consider the gender-specific social implications of agoraphobic self-disclosure. Men may be less inclined to acknowledge agoraphobic tendencies than women because it discredits male strength and bravery (Barlow, 1988). This is believed by some to contribute to the disparate rates of agoraphobia diagnoses in men and women, and it is presumed that there is a group of "hidden male agoraphobics" who tend to present with alcoholism. There is some empirical support for this. In a study of gender-specific alcohol use in agoraphobic individuals, there were significant sex differences in the ways in which each gender described the experience of the anxiety disorder (Cox et al., 1993): males consumed significantly more alcohol than females and they described their drinking as a specific coping strategy for the anxiety. Turgeon and colleagues (1998) did not confirm this quantitative difference and found comparable alcohol consumption in male and female samples. However, in both studies, males and not females directly reported drinking as a way to decrease agoraphobic inhibition (Cox et al., 1993; Turgeon et al., 1998).

Social phobia

Social anxiety disorder (SAD) affects the sexes almost equally with approximately 15% of women and 11% of men affected across the life-course. (Kessler et al., 2005). SAD usually begins in childhood or early adolescence and maintains a chronic course throughout adulthood. The clinical features include experiencing extreme anxiety in social scenarios due to a fear of embarrassment. The feared situation is either endured with difficulty or avoided altogether, and the fear and avoidance behavior leads to disability in functioning. Sufferers often manifest physical signs such as blushing and stuttering if asked to speak in public. They may become avoidant of social situations and there is some difference between with sexes with women stating that they have more distress when speaking in public or meeting strangers (Turk et al. 1998).

In the NCS, the 1-year prevalence of social phobia was 6.6% (se=0.4) in men and 9.1% (se=0.7) in women

(Kessler et al., 1994). The lifetime risk for males was 11.1% (se=0.8) while for females it was 15.5% (se=1.0). Slightly lower lifetime rates (13.7%) were found in an epidemiological study from Ontario, Canada, but a 2:1 ratio for females compared to males was noted (DeWit, 1999). A community study in Australia found that women were only slightly more likely than men to develop the illness (Lampe et al., 2003).

Possible sex differences in the expression of social phobia have been investigated in clinical cohorts. Male (n=108) and female (n=104) subjects with social phobia differed somewhat in the fearful situations they endorsed (Turk et al., 1998). Severity was significantly greater for women compared to men for the following tasks: talking to an authority, acting or speaking in front of an audience, being observed at work, entering into a room while others were seated, being the center of attention, expressing disagreement and giving a party (Turk et al., 1998). Men had significantly more difficulty with urinating in public and returning goods to a store. An independent study also found that socially phobic women had more difficulty than men with speaking in public (Pollard & Henderson, 1988).

One small study suggests sex differences in the psychophysiological response to stress among people with social phobia (Grossman et al., 2001). Women with social phobia were more likely than men with the disorder to show an increase in heart rate and both diastolic and systolic blood pressure in response to speech stress.

Comorbidity

Social phobia is commonly comorbid with other conditions, particularly panic disorder, generalized anxiety disorder, major depressive disorder, obsessive-compulsive disorder and agoraphobia (Yonkers, 2001). In most instances, social phobia is temporally primary (Yonkers et al., 2001).

Clinical course

Social phobia typically begins during adolescence (~age 16) with a predominance of girls over boys (Compton et al., 2000). Several studies document the chronicity associated with the condition (DeWit et al., 1999; Yonkers et al., 2001). The clinical course appears to be similar in men and women (Yonkers et al., 2001); however, those individuals with an early age of onset are less likely to recover than those with a later onset.

Obsessive-compulsive disorder

Obsessive-compulsive disorder (OCD) is characterized by intrusive thoughts (obsessions) and compulsive activities that attenuate (at least in the short term) the level of anxiety associated with the obsession. The condition is associated with considerable distress and impairment of daily activities, with (by definition) at least 1 hour per day being expended on rituals.

Increasingly, OCD is recognized as a fairly common and disabling condition, estimated to have been the fifth leading cause of disability for women aged 15–44 years, in developed countries in 1990 (Murray & Lopez, 1996). Most epidemiological surveys suggest that the condition afflicts women at a somewhat higher rate than men. Bebbington (1990) reviewed population-based studies of OCD, and found a female:male ratio varying from 0.9:1 (Puerto Rico) to 3.4:1 (Christchurch, New Zealand). He concluded that overall females appear somewhat more prone to the condition, with an overall relative risk of 1.5, compared to men. Clinical samples tend to show a somewhat less marked female excess, perhaps a reflection of the rather more severe illness course in men or differences in help-seeking behavior (Castle et al., 1995; Lensi et al., 1996; Noshirvani et al., 1991).

What certainly seems consistent in the literature is that males tend to have an earlier onset of OCD than their female counterparts. For example, in a clinical series of 307 OCD patients (55% female), onset of illness for males was 21 while it was 24 years for females (p<0.01) (Noshirvani et al., 1991). Similar discrepancies in onset have been reported by other researchers (Castle et al., 1995; Lensi et al., 1996; Lochner et al., 2004). What is also consistent is that early-onset samples of OCD show a preponderance of males. In a review of eight studies of child- and adolescent-onset OCD, there was a total of 174 boys and 70 girls, yielding a gender ratio of 5:2 (Noshirvani et al., 1991).

This is also reflected in case series across all ages of onset; for example, Castle et al. (1995) found males were overrepresented amongst patients with an onset of illness before 16 years (26% vs. 12% of females; p=0.01).

In terms of symptom profile, women with OCD are generally more likely that men to manifest contamination fears and cleaning rituals, while males are more prone to aggressive and sexual obsessions, and symmetry concerns (Lensi et al., 1996; Bogetto et al., 1999).

Women with OCD often report that symptoms first appear or exacerbate during reproductive cycle events and recent research has demonstrated the relationship between OCD and the reproductive cycle in women. A meta-analysis (Russell et al., 2013) found that the prevalence of OCD increased during pregnancy (mean = 2.07%) and even more so in the postpartum period (mean = 2.43%) compared with the general population (mean = 1.08%). Additionally, both pregnant (mean = 1.45) and postpartum (mean = 2.38) women were at greater risk of experiencing OCD compared to the general female population, with an aggregate risk ratio of 1.79 (Russell et al., 2013).

Further research has focused on OCD across the reproductive cycle including at menarche, premenstruum, pregnancy, postpartum and at menopause (Gulielmi et al., 2014). In a survey of 542 women (United States, n=352; Netherlands, n=190) using a self-report questionnaire of symptoms across time, a significant relationship between exacerbations of OCD and various phases of the reproductive cycle was found. OCD onset occurred within 12 months of menarche in 13.0% of participants, during pregnancy in 5.1%, postpartum in 4.7% and at menopause in 3.7%. It was evident that worsening of preexisting OCD occurred at reproductive cycle stages with 37.6% of women reporting worsening of symptoms at premenstruum, 33.0% during pregnancy, 46.6% in postpartum period, and 32.7% at menopause. Furthermore, OCD during a first pregnancy was significantly associated with exacerbation in a second pregnancy (OR = 10.82, 95% CI 4.48–26.16); similarly, postpartum exacerbation in a first pregnancy was associated with an elevated risk in ensuing pregnancies (OR = 6.86, 95% CI 3.27–14.36). These findings reinforce the importance of clinical vigilance during these phases of the reproductive cycle (Guglielmi et al., 2014).

Comorbidity

Females with OCD are more likely than their male counterparts to suffer from depression or eating disorders, but males appear more vulnerable to later hypomania (Lensi et al., 1996; Bogetto et al., 1999). Furthermore, males with OCD, and particularly those with an early onset illness, are more likely to exhibit motor tics and neurological "soft signs" (see Blanes & McGuire, 1997).

Clinical course

Most (though not all; Lensi et al., 1996) case series suggest a more benign longitudinal course for OCD amongst women, with a more abrupt onset and more episodic course (Bogetto et al., 1999). Women with OCD are also more likely to be married and to have less impairment of psychosocial functioning.

Whether the relatively more benign course of illness in women is due to the late mean age at onset, or is a reflection of a male vulnerability to a particularly pernicious subtype of the illness, is not clear. One hypothesis is there is a male-predominant "neurodevelopmental" subtype of OCD, characterized by an early onset of illness, neurological soft signs, motor tics and a poor treatment response to serotonergic antidepressants (see Blanes & McGuire, 1997)

Another interesting line of enquiry has been into the possibility that genetic factors might play a differential role between the sexes, in terms of OCD. For example, Enoch et al. (2001) reported the frequency of 5-HT2A promoter polymorphism 1438G>A to be higher among OCD women but not men, versus a comparison group. Of interest is that this polymorphism had been found previously to be associated with anorexia nervosa, believed by some researchers to be part of an OCD spectrum of disorders. Lochner et al. (2004) found that Caucasian females (but not males) with OCD were more likely than those in a comparison group to have the high activity T allele of the EcoRV variant of the monoamine oxidase A gene. These lines of genetic enquiry need to be pursued further and to be intergrated into broader explanatory models of gender differences in OCD.

Influences of the menstrual cycle on anxiety symptoms

Several researchers note high rates of anxiety disorders in their patients with Premenstrual Dysphoric Disorder (PMDD) (Facchinetti et al., 1992; Fava et al., 1992) with the most common diagnosis being panic disorder. Sexual trauma history seems prevalent in PMDD patients. In one study of 42 women (Golding et al., 2000), 95% had experienced sexual trauma at least once; upon further assessment, 65% were diagnosed with PTSD.

Worsening of panic during the premenstrual week is endorsed by many women with panic disorder. However, research has failed to confirm worsening

panic when daily calendars are used to evaluate menstrual cycle symptoms prospectively (Cameron et al., 1988; Cook et al., 1990; Stein et al., 1989). However, some studies have identified anxiety as a key problematic symptom prior to the onset of menses (Stein et al., 1989). PMDD is clinically categorized as a depressive mood disorder, but further evaluation is required to understand the anxious quality of the disorder better (see also Chapter 10).

There is additional information suggesting a link between premenstrual conditions and anxiety disorders. In a study of women seeking treatment for premenstrual dysphoria (n=206), they prospectively rated their daily symptoms (Bailey and Cohen, 1999). According to the Structured Clinical Interview for DSM (SCID), 7.3% (n=15) were diagnosed with solely an anxiety disorder. A further 8.2% (n=17) had both an anxiety and a mood disorder; by far the most common diagnosis was panic disorder (n=18). Furthermore, 20 undiagnosed women were already receiving treatment for a mood or anxiety disorder, possibly minimizing identification of current illness. In a clinical sample of female patients presenting for treatment for PMDD, approximately 20% had a co-occurring Axis I anxiety disorder (Yonkers, unpublished data, 2004).

Perinatal anxiety disorders

Early studies of pregnant patients with a history of panic disorder observed an overall improvement in the illness during pregnancy (Levine et al., 2003). Studies are limited and subsequent studies have mixed findings. Retrospective studies find that the course of illness had an equal likelihood of improving, worsening or remaining unchanged during the course of pregnancy (Cohen et al., 1994, 1996; and see Chapter 10); the postpartum period offers no greater certainty of symptom abatement, and in fact is a time when some women experience the first manifestation of panic disorder. Indeed, new onset of postpartum panic disorder seems to afflict between 11 and 33% of pregnant women (Levine et al., 2003). On the other hand, recent retrospective work suggests improvement in panic over the course of pregnancy (Yonkers, unpublished data, 2014). A review found that postpartum improvement in panic episodes was most notably due to medication treatment (Levine et al., 2003). In one cohort of patients with panic disorder, 90% were symptomatic in the immediate postpartum

period (Cohen et al., 1996); the asymptomatic 10% of patients were all taking medication to treat their panic disorder.

Research that assessed rates of panic disorder and PTSD in a prenatal sample (n=387) in primary care found a rate of panic disorder during pregnancy was 2%, and the rate of PTSD, 3% (Smith et al., 2004). Rates of detection by these women's obstetricians were low, although rates of treatment were high, such that at the time of the study's contact with the anxious patients, all of the women with panic disorder (n=9) were currently or had previously been engaged in treatment, while 50% of the women with PTSD (n=5) were currently or had previously been treated. While these sample sizes are small, the rates of participation in treatment are encouraging.

As noted earlier, pregnancy and the postpartum period can be times of worsening or onset of OCD (Brandes et al., 2004; Levine, et al., 2003). Current data suggest that an OCD patient has little hope for symptomatic reprieve during pregnancy or postpartum (Altshuler et al., 1998; Levine et al., 2003). Of particular concern in the postpartum population are intrusive and unwanted thoughts, impulses and images of harming the infant. These thoughts could occur as symptoms of OCD and/or as indicators of postpartum depression, raising particular challenges for clinicians (see Chapter 10).

Pregnancy is protective against the continuous expression of symptoms of GAD (Buist et al, 2011). Nearly one-half of women with GAD in the 6 months prior to pregnancy experienced a remission in pregnancy (Buist et al 2011). Women were less likely to remit if they were older than age 35 as compared to 25–34, had a college education as compared to high school degree, experienced multiple prior episodes of GAD, had low social support and a history of child abuse.

A study of self-reported anxiousness during the postpartum period (not diagnosable anxiety disorder per se) suggested a common occurrence of comorbid anxiety and depression in the postpartum period (Stuart et al., 1998). The sample consisted of 107 community volunteers, primarily Caucasian, married and employed. Self-reported anxiety increased over time in this sample, reaching 8.7% at 14 weeks postpartum and increasing to 16.8% at 30 weeks. One could loosely parallel this to generalized anxiety, although no formal axis I diagnoses were made. It is unknown for this sample whether their anxiety was being

treated, and/or whether they had a history of anxiety or depressive disorder during pregnancy or perhaps even prior to gestation. The findings do suggest, however, a high index of suspicion amongst clinicians working with postpartum women, such that anxiety symptoms are recognized and appropriately dealt with. For a more detailed discussion, the reader is referred to Chapter 10.

Anxiety disorders in older women

Anxiety disorders tend to show a reduction in prevalence as people age, but rates remain higher in women than in men (Byers et al., 2010). For women in mid-life, a history of anxiety is a most significant predictor of reduced quality of life, an effect that is not explained by the sleep disturbance associated with these disorders (Joffe et al., 2012).

In a recent systematic review, examining 19 studies conducted between 1960 and 2011, Bryant et al. (2012) evaluated the prevalence of anxiety disorders during the menopausal transition to ascertain whether there was any utility in the diagnosis of "menopausal anxiety" as a discrete category. The review examined the relationship between the vasomotor symptoms of menopause, for example "hot flushes," and anxiety states and they suggested that

in studying these symptoms it is essential that physiological and psychological symptoms are not confounded through the use of inappropriate outcome measures. The authors determined that there is no current evidence to suggest that there is an increased prevalence of anxiety disorders during menopause, nor the emergence of an anxiety disorder specifically determined by menopause.

For a discussion about anxiety disorders in post-menopausal women, the reader is referred to Chapter 20 of this book.

Conclusions

Women are disproportionally afflicted by all the anxiety disorders and as yet there are few firm findings as to why women remain more susceptible than men. Research concentrating on the relationship between early life traumatic events, heritable genetic predisposition to anxiety disorders and the influence of the menstrual cycle on anxiety disorders are all areas that require further elaboration. Given the early onset of anxiety disorder, studies evaluating gender and risk will need to include investigations in children and adolescents. Further work is also required into gender-informed treatments across the life-course.

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