Gender Differences in the Rates of Exposure to Stressful Life Events and Sensitivity to Their Depressogenic Effects

Kenneth S. Kendler, M.D. Laura M. Thornton, Ph.D. Carol A. Prescott, Ph.D. **Objective:** Women are at greater risk for major depression than men. The authors sought to determine whether the gender difference in prevalence for major depression was due to more frequent exposure to stressful life events and/or greater sensitivity to their depressogenic effects.

Method: Male-male, female-female, and male-female twin pairs from a population-based registry were personally interviewed. Each interview assessed the occurrence, to the nearest month, of 18 personal and social network classes of stressful life events and episode onsets of major depression. Standard logistic regression analyses were conducted for the same-sex pairs, and each female twin in the opposite-sex pairs was compared with her male co-twin by using conditional logistic regression.

Results: Women consistently reported higher rates of housing problems, loss of confidant, crises and problems getting along with individuals in their proximal network, and illness of individuals within their distal network. In both the same-sex

and opposite-sex samples, men reported higher rates of job loss, legal problems, robbery, and work problems. Consistent sex differences in the depressogenic effect of stressful life events were seen for three event categories: men were more sensitive to the depressogenic effects of divorce or separation and work problems; women were more sensitive to the depressogenic effects of problems getting along with individuals in their proximal network. None of the gender difference in prevalence of major depression could be explained by differing rates of or sensitivities to stressful life events.

Conclusions: Women reported more interpersonal whereas men reported more legal and work-related stressful life events. Most life event categories influenced the risk for major depression similarly in the two sexes. The results suggest that the greater prevalence of major depression in women versus men is due neither to differences in the rates of reported stressful life events nor to differential sensitivity to their pathogenic effect.

(Am J Psychiatry 2001; 158:587-593)

wo of the most widely replicated findings for major depression are its greater prevalence in women after adolescence (1–3) and its causal association with stressful life events (4–8). The goal of this study was to further our understanding of how these two sets of findings are interrelated. In particular, do the genders differ in their rate of exposure to stressful life events or in their sensitivity to the depressogenic effects of these events?

Three patterns of association between gender and life event *exposure* are most commonly seen in the literature:

1) women have a broadly higher risk for most or all categories of stressful life events (9, 10); 2) women are at greater risk for a subset of events (e.g., network, interpersonal) (11–13); and 3) no major differences are seen between the genders in event exposure (14–17). An analysis of six event categories obtained in questionnaire form from five prior general population studies (18) provided a more complex result: men reported more income-related events, whereas women reported more network events. Most of these studies had several noteworthy limitations, including modest sample sizes, limited range of event

categories, assessment of events by self-report checklist, and sampling solely from clinical sources, with the associated possible biases.

Previous studies have also produced a range of findings about gender differences in sensitivity to stressful life events (19). Most, but not all (20, 21), of these studies have employed self-report measures of "depression" or "distress," rather than syndromal diagnoses of major depression. The majority of studies have reported a greater sensitivity to the pathogenic effect of stressful life events in women that is either global (22) or restricted to certain events, including problems in social relationships (23) or children, housing, or reproductive problems (21). Two studies examined the "perceived stressfulness" of stressful life events: one found stressfulness to be higher for women in general (13), and one reported no gender difference (15). However, some evidence of greater male sensitivity has also been reported. A large, longitudinal study of adolescents showed a greater impact of prior stressful life events on internalizing symptoms in boys than girls (24), and in an analysis of the Epidemiologic Catchment Area study, men had a higher rate of initial major depressive onsets that were associated with marital disruption (20). The analysis of five previous population studies found women to be more sensitive to the depressogenic effects of network events and death of a loved one, whereas men were more sensitive to income loss (18).

Using methods that addressed many of the weaknesses of prior studies, we examined in two large, general population twin samples three specific questions:

- 1. Do men and women differ in their rates of exposure to various classes of stressful life events?
- 2. Do men and women differ in their vulnerability to the depressogenic effects of various classes of stressful life events?
- 3. What contribution do any differences in exposure or sensitivity to stressful life events make to the overall gender difference in rates of major depression?

Method

Sample

The twins in this study came from two interrelated projects that used the population-based Virginia Twin Registry (25)formed from a systematic review of all birth certificates in the Commonwealth of Virginia—which now constitutes part of the Mid-Atlantic Twin Registry. The female-female twin pairs used in this study were born during the years 1934-1974. In these studies, signed informed consent was obtained before all face-to-face interviews and verbal assent before all telephone interviews. Twin pairs became eligible to participate if both members had previously responded to a mailed questionnaire, the response rate to which was approximately 64%. Eighty-eight percent of this sample was first interviewed face-to-face in 1987-1989 and has subsequently been the subject of three additional telephone interview waves. The remainder of our female-female twin sample was first interviewed face-to-face in 1992-1994 (counted as part of our wave 1) and interviewed a second time (as part of our wave 4 assessment) by telephone in 1996 and 1997. At the fourth wave, the mean age and level of education of the sample were 36.3 (SD=8.2) and 14.3 (SD=2.2) years, respectively. Marital status was as follows: married=66.7%, divorced or separated=12.8%, widowed= 0.9%, never married=19.6%. The proportion of twin pairs that were monozygotic was 60.7%.

The total number of twins from the female-female pairs who participated in any wave was 2,395. The number of individuals (and resulting person-months) for each of the four assessment waves was as follows: wave 1: N=2,164 (28,121 person-months); wave 2: N=2,003 (26,039 person-months); wave 3: N=1,899 (24,687 person-months); and wave 4: N=1,943 (25,259 personmonths). Cooperation across assessment waves ranged from 85% to 92% (25) and was significantly predicted by years of education (χ^2 =41.4, df=1, p<0.0001) but not by marital status (χ^2 =1.83, df=3, p=0.60). All assessments were separated by at least 13 months.

The male-male and male-female twin pairs, born during the years 1940–1974, were ascertained in a separate study that began in 1993 (details outlined elsewhere [25]) in which we succeeded in interviewing by telephone 72% of those eligible. This sample was followed up with a second wave of interviews (79.4% of which were completed face-to-face) with a mean between-interview interval of 19 months (SD=9, range=12–65). Again, cooperation across waves was predicted by years of education but not by marital status (χ^2 =113.9, df=1, p<0.0001, and χ^2 =1.0, df=3, p=0.80, respectively). At the second wave, the mean age and level of educa-

tion of the sample were 37.0 (SD=9.1) and 13.6 (SD=2.6) years, respectively. Marital status was as follows: married=69.6%, divorced or separated=10.2%, widowed=0.5%, never married=19.7%. For the purposes of this study, this group was subdivided into male-male and male-female pairs. The number of individuals (and resulting person-months) for each of the two waves was as follows: wave 1: N=3,526 (45,838 person-months); wave 2: N=2,927 (38,051 person-months). The total number of twins from male-female pairs who participated in any wave was 3,312. The number of individuals (and resulting person-months) for each of the two waves was as follows: wave 1: N=3,310 (43,030 person-months); wave 2: N=2,714 (35,282 person-months). The proportion of malemale pairs in the second wave who were monozygotic was 58.9%.

Measures

At each interview, using items adapted from the Structured Clinical Interview for DSM-III-R (26), we assessed the occurrence over the last year of 14 individual symptoms that represented the disaggregated nine "A" criteria for major depression in DSM-III-R (e.g., separate items to assess insomnia and hypersomnia). For each symptom that the subject reported, interviewers probed to ensure that it was due neither to physical illness nor medication. The respondents and interviewers then had to aggregate symptoms reported over the last year into co-occurring syndromes. If depressive syndromes occurred, respondents were asked the months of their onset and offset. The diagnosis of major depression was made by a computer algorithm that used DSM-III-R criteria (except criterion B2, which excludes "uncomplicated bereavement").

In earlier sections of the interview, we assessed the occurrence, to the nearest month, of 11 "personal" events (events occurring primarily to the informant): assault (e.g., rape or mugging), divorce or separation (which could also include broken engagement or breakup of other romantic relationship), major financial problems, serious housing problems, serious illness or injury, job loss (either being laid off or fired), legal problems (covered trouble with police and other legal difficulties), loss of confidant (separation from other loved one or close friend other than spouse/ partner), serious marital problems (could involve a marriage-like intimate or one with whom the subject was in a cohabiting relationship), robbery, or serious difficulties at work. We also assessed four classes of "network" events (events that occurred primarily to, or in interaction with, an individual in the respondent's social network): serious trouble getting along with an individual in the network, a serious personal crisis of someone in the network, death of an individual in the network, or serious illness of someone in the network. Because of prior evidence that women may be more sensitive than men to events occurring to individuals further out in their social networks (27), we divided the social network of the twins into proximal and distal. Proximal members of the network included the respondent's spouse, child, parent, cotwin, and other nontwin siblings. Distal members of the network fell into two categories: "other close relative" or "someone else close to you." Information was lacking on crises involving individuals within the distal network.

Not all individuals in our sample were susceptible to all stressful life event categories. Those who were not working could not experience job loss or work problems. Those who were not married or living with an intimate partner could not experience marital problems. Information on work status was only available from waves 1 and 4 in the female-female twin pairs and from wave 2 for the male-male and opposite-sex pairs. Analyses were repeated on these waves of data, censoring individuals who were not working or not married. This resulted in a loss of power that was particularly acute in the opposite-sex sample, since a pair was dropped from the analysis if either member was not working or not married.

Statistical Analysis

Our sample contained two kinds of data for the analysis of gender differences. As typical in other samples, our same-sex pairs could be compared controlling for age. However, with our opposite-sex pairs we could compare each sister with her twin brother, capitalizing on the fact that these sibling pairs are perfectly matched on many variables of interest (e.g., age, social class of rearing, parental personality, other aspects of the home environment).

We conducted an event history analysis using a discrete-time approach, examining each person-month of observation. The observations contained information about which stressful life events occurred, whether an episode of major depression started in that month, age of the subject at the time of the interview, and the hazard rate of depression to correct for unequal distribution of onsets within the study year. Person-months were deleted from the sample if the subject was in an episode of depression that began before the month in question.

We first examined whether there was a gender difference in occurrence/reporting of life events. In the same-sex twin pairs, we used logistic regression (28) as operationalized in PROC LOGIS-TIC in SAS (29) to predict the life event from gender. In the opposite-sex pairs, we took advantage of the "pairedness" of the data and applied conditional logistic regression (28) as operationalized using PROC PHREG with the STRATA option, matching by family (29). For each twin pair, the set of person-months for the female twin was matched with the set of person-months of the male twin, giving an M \times N design while correcting for the non-independence of the data. Because the subjects are paired by family and this analysis is similar to a case-control type study, the regression model is specified in the "nonintuitive" direction: sex (the case-control variable) is the dependent measure, and stressful life event is specified as the independent measure.

Second, we examined whether a depressive onset occurred more frequently in one sex than in the other in relation to a particular life event. For these analyses in the same-sex twin pairs, we again applied PROC LOGISTIC to the data, predicting depressive onset from the stressful life event, sex, and the interaction between stressful life event and sex. Age, hazard rate of depression, and dummy variables accounting for differences between interviews in answers to questions about the life events (if any) were entered into the model as covariates. In the opposite-sex sample, conditional logistic regression was again applied, with the dependent measure necessarily being sex and the predictors being depressive onset, life event, and the interaction between depressive onset and life event.

We used our same-sex pairs as a "test" sample, using traditional two-tailed p values. Our opposite-sex pairs were treated as a "replication" sample. If the results were in the same direction as a significant result from the test sample, then one-tailed tests were used.

Results

Gender and the Frequency of Stressful Life Events

The association between gender and the frequency of 18 stressful life events in both our "test" sample of same-sex twin pairs and the "replicate" sample of opposite-sex twin pairs, in the form of odds ratios and their 95% confidence intervals (CIs), is shown in Table 1. On the basis of these results, the 18 stressful life events can be classified into three categories:

1. Male-preponderant. There were four stressful life events in which men reported significantly higher rates of occurrence than women in both the same-sex and opposite-sex twin samples: job loss, legal problems, robbery, and work problems.

- 2. Female-preponderant. Women reported significantly higher rates of five stressful life events in both the same-sex and the opposite-sex twin samples: housing problems, loss of confidant, problems getting along with and crises involving individuals in their proximal network, and illness of an individual in their distal network.
- 3. No or inconsistent gender difference. For six stressful life events, no consistent pattern of gender differences in their occurrence rate was seen across the two samples: financial problems, marital problems, illness, illness of individual in one's proximal network, and problems getting along with and death of an individual in one's distal network. For three events (assault, divorce or separation, and death of an individual within the proximal network), men reported significantly higher rates in the same-sex twin sample, but the results in the opposite-sex sample, while in the same direction, were not significant.

We reanalyzed data for the three event categories for which some individuals in the sample were not susceptible: job loss, work problems, and marital problems. For job loss, the pattern of results changed appreciably. Among those currently employed, women reported nonsignificantly higher rates of job loss in both the same-sex twin sample (odds ratio=1.16, 95% CI=0.93–1.44; χ^2 =1.64, df=1, p=0.20) and the opposite-sex twin sample (odds ratio= 1.12, 95% CI=0.59–2.13; χ^2 =0.12, df=1, p=0.72). For work problems, the results were less clear. Among those who were employed, men still reported more work-related problems in both samples. This difference approached significance in the same-sex twin sample (odds ratio=0.87, 95% CI=0.74–1.02; χ^2 =3.13, df=1, p=0.07) and was similar in magnitude but not significant in the opposite-sex twin sample (odds ratio=0.91, 95% CI=0.71-1.17; χ^2 =0.56, df=1, p=0.45). Among those who were married, women reported significantly more marital problems in the same-sex twin sample (odds ratio=1.19, 95% CI=1.01–1.40; χ^2 =4.52, df=1, p=0.03). However, no such relationship was seen in those opposite-sex pairs where both were married (odds ratio= 1.02, 95% CI=0.73–1.41; χ^2 =0.01, df=1, p=0.92).

Gender and Sensitivity to the Depressogenic Effect of Stressful Life Events

Table 1 also depicts the odds ratios and confidence intervals for the interaction between gender and individual stressful life events in predicting the onset of major depression in the two samples. Again, we can usefully classify the 18 stressful life events into three classes:

- 1. Male-sensitive. Men were significantly more sensitive than women to the depressogenic effects of two stressful life events in the "test" sample: divorce or separation and work problems. Both of these results were replicated in the opposite-sex twin sample.
- 2. Female-sensitive. In the same-sex twin sample, women were significantly more sensitive than men to the

TABLE 1. Gender Differences in Exposure to 18 Stressful Life Events and Sensitivity to Their Depressogenic Effect in Two Twin Pair Samples

	Same-Sex Twin Pairs				Opposite-Sex Twin Pairs			
Stressful Life Event	Exposurea		Sensitivity ^b		Exposurea		Sensitivity ^b	
	Odds Ratio ^c	95% CI	Odds Ratio ^c	95% CI	Odds Ratio ^c	95% CI	Odds Ratio ^c	95% CI
Assault	0.70*	0.52-0.93	3.18	0.87-11.61	0.65	0.39-1.10	1.93	0.28-13.50
Divorce or separation	0.85***	0.77-0.93	0.56***	0.40 - 0.77	0.95	0.81-1.11	0.50**	0.29 - 0.87
Financial problems	0.41†	0.38 - 0.44	1.29	0.86 - 1.92	1.02	0.93 - 1.13	0.87	0.48 - 1.56
Housing problems	1.41***	1.17-1.71	1.39	0.51 - 3.82	1.34*	0.95-1.88	0.38	0.10-1.42
Illness	1.03	0.96-1.11	1.03	0.64-1.63	1.26***	1.12-1.42	1.45	0.79 - 2.65
Job loss	0.84*	0.74 - 0.96	0.72	0.37 - 1.40	0.68**	0.51 - 0.90	0.18*	0.04-0.93
Legal problems	0.59†	0.48 - 0.72	0.53	0.21 - 1.33	0.60***	0.45 - 0.81	0.96	0.34 - 2.72
Loss of confidant	1.30†	1.20-1.42	1.25	0.76 - 2.05	1.41†	1.29-1.63	0.72	0.37-1.37
Marital problems	0.98	0.87 - 1.09	0.98	0.63 - 1.53	1.12	0.94-1.35	1.12	0.59 - 2.16
Robbery	0.81**	0.70 - 0.94	1.20	0.31-4.59	0.75*	0.58 - 0.96	3.86	0.42-34.50
Work problems	0.80†	0.73 - 0.88	0.51**	0.31-0.83	0.83**	0.72 - 0.96	0.36**	0.15-0.84
Proximal network event ^d								
Problems in getting along	1.18***	1.08-1.29	1.65*	1.01-2.71	1.37†	1.18-1.58	2.22*	1.11-4.24
Crisis	1.42†	1.34-1.48	0.98	0.70 - 1.38	1.18†	1.08-1.28	0.66	0.42 - 1.03
Death	0.77**	0.65-0.91	2.37*	1.07-5.26	0.94	0.70 - 1.27	1.64	0.62 - 4.37
Illness	0.97	0.91 - 1.04	1.38	0.86 - 2.23	1.16**	1.05-1.30	0.88	0.42 - 1.86
Distal network event ^e								
Problems in getting along	1.02	0.93 - 1.12	0.84	0.51 - 1.40	1.21*	1.04-1.41	1.17	0.49 - 2.75
Death	0.97	0.91-1.04	1.38	0.82 - 2.32	1.00	0.91-1.11	0.74	0.37-1.47
Illness	1.16†	1.08-1.25	1.79	0.87 - 3.67	1.17**	1.03-1.33	0.91	0.32 - 2.58

^a Analyses used standard logistic regression (same-sex sample, df=1) or conditional logistic regression analyses (opposite-sex sample, df=1) to predict exposure or reporting of event based on gender.

depressogenic effects of problems getting along with and death of an individual in their proximal network. Only the results for problems getting along with a proximal network individual were replicated in the opposite-sex twin sample.

3. No consistent gender difference in sensitivity. Across samples, no consistent and significant gender differences were seen in the sensitivity to the remaining 15 event categories. Three nonsignificant findings are noteworthy. First, women were substantially, but nonsignificantly, more sensitive to the depressogenic effects of assault in both samples. Power is low in this event category because of its rarity. Second, a very large and significant difference was seen in greater male sensitivity to the effect of job loss in the opposite-sex sample, but this difference was much more modest and nonsignificant in the same-sex sample. Third, as previously noted, women were significantly more sensitive to the effects of death of an individual in their proximal network in the same-sex twin sample; a similar but nonsignificant finding was seen in the opposite-sex sample.

Accounting for Gender Differences in the Risk for Major Depression

In the same-sex twin sample, the odds ratio for risk for onset of major depression in any month in women versus men was 2.19. This odds ratio did not change appreciably when we added, as covariates, all 18 stressful life event categories (odds ratio=2.22) or when we, in addition, added the interaction between gender and each individual event

category (odds ratio=2.20). It is interesting to note that in the opposite-sex twin pairs, the association between gender and risk for major depression was considerably more modest than that seen in the same-sex pairs, producing an odds ratio of 1.37. This odds ratio did not change appreciably when we added all 18 stressful life event categories as covariates (odds ratio=1.38) and actually increased modestly when we also added the interaction between gender and each individual event category (odds ratio=1.45).

Discussion

While women consistently reported higher exposure rates to certain stressful life events (housing problems, loss of confidant, crises and problems getting along with individuals in their proximal network, and illness of individuals in their distal network), men consistently reported higher rates of other stressful life events (job loss, legal problems, robbery, and work problems). Consistent sex differences in the sensitivity to stressful life events were seen for only three event categories: men were more sensitive to the effect of divorce or separation and work problems, and women were more sensitive to the impact of problems getting along with individuals in their proximal network. Gender differences in the prevalence rate of major depression could not be explained by differences in rates of exposure or sensitivities to stressful life events.

Our results are inconsistent with the hypothesis that the genders differ in any overall liability to experience or re-

^b Analyses used standard logistic regression (same-sex sample, df=1) or conditional logistic regression analyses (opposite-sex sample, df=1). The odds ratio reflects the prediction of the onset of major depression by the interaction between gender and stressful life event.

^c Values less than 1.00 indicate events more likely ascribed to men; values greater than 1.00 indicate events more likely ascribed to women.

^d Involves the subject's spouse, child, parent, co-twin, or nontwin sibling.

e Involves individuals the subjects classified as being a close relative (but outside of the proximal network) or someone close to them.

^{*}p<0.05. **p<0.01. ***p<0.001. †p<0.0001.

port stressful events. However, significant differences in exposure to specific event types, replicated across both samples, were found for nine of the 18 assessed event categories. Consistent with some prior work (11-13, 18), four of the five events that occurred more commonly to women were either network or interpersonal events. Our data do not permit us to determine whether these findings stem from women having larger networks or being more sensitive to the adversities that occur in their networks. However, women did not report death of an individual from their proximal or distal network more frequently than men, suggesting that sensitivity to events less traumatic than death rather than network size may discriminate the genders. Our results did not provide support for the hypothesis that the gender differences in the rates of reported stressful life events are greater in the distal than the proximal social network (27).

In both samples, men reported significantly more frequent exposure to four event categories that reflected greater risk for occupationally related (job loss and work problems) and law/violence-related (robbery and legal problems) stressors. Of note, male excesses in reports of assault were similar to that seen for robbery but were significant only for the same-sex sample. Men appear to report higher rates of job loss solely because they are more frequently employed, but this could not entirely explain the male excess of work problems. Our results are consistent with those of a large-sample study in adolescents in which male subjects reported significantly higher rates of events associated with "deviant" behaviors, such as getting in trouble with the law or at school and stealing (12).

Our results suggest that neither gender has a generally increased liability to experience or report stressful events. However, a number of differences are seen in the rates of individual event categories in men and women, the pattern of which is consistent with the expectations given the general gender roles in our society (30).

In our data, we found no evidence for an overall gender difference in sensitivity to the depressogenic effects of stressful life events, finding reliable gender differences across both samples in only three of 18 event categories. Contrary to most but not all previous studies, two out of the three significant differences reflected a greater male sensitivity to stressful life events. We replicated prior evidence for greater male sensitivity to the depressogenic effects of divorce or separation (20), which may parallel the greater mortality seen in widowers than widows (31). The two other significant differences—greater male sensitivity to work problems and greater female sensitivity to problems getting along with individuals in their proximal social network—are consistent with previous evidence that women are generally more invested in interpersonal relationships, whereas men are more involved in occupational success (32, 33). Although some other patterns in the data are supportive of this hypothesis (e.g., inconsistent evidence across the samples that men are more sensitive to

the effects of job loss and women to the effects of death in the proximal network), others clearly are not (e.g., inconsistent evidence that men are *more* sensitive to crises in the proximal network and no clear evidence for greater female sensitivity to loss of confidant, marital problems, or illness in the proximal or distal network). In aggregate, our data suggest that the similarities in men and women in their sensitivity to the depressogenic effect of stressful life events considerably outweigh their differences.

We are aware of two studies, both employing self-report scales of depressive symptoms, that found that 30%-78% (18) and 25% (34) of the gender differences in depression could be accounted for by gender differences in the exposure to and sensitivity to stressful life events. Using interview-based assessments of both stressful life events and the onset of clinically defined major depression, we were unable to replicate these findings. In both our data sets, gender differences in the frequency of reported stressful life events and sensitivity to their depressogenic effects could account for virtually none of the female preponderance in prevalence rates for major depression. More specifically, our data are inconsistent with the "cost of caring" hypothesis, in which higher rates of major depression in women result from women both having larger social networks than men and being more affected by events in their network (27). Bebbington concluded from his careful review on gender differences in major depression that "social and psychological disparities appear to be the most important determinants of the sex difference" (27). Our results do not provide support for the hypothesis that gender differences in the social and psychological processes that reflect exposure to or reactivity to stressful life events play a major role in explaining the higher rates of major depression in women.

These results need to be interpreted in the context of the strengths and limitations of this study. Several strengths are noteworthy. The sample size was large. Both stressful life event occurrence and depressive onsets were assessed by clinically trained interviewers. A wide range of stressful life events was assessed. We used two independent samples, one of which was relatively unique. By comparing event occurrence and sensitivity in opposite-sex twin pairs, we were able to match individuals who, while different in gender, were born at the same time into the same family and would therefore have had highly correlated exposures to family and community factors that might influence their risk for stressful life events and major depression.

Six limitations are noteworthy. First, our sample was entirely composed of Caucasian twins born in Virginia. These findings may not extrapolate to other ethnic groups or different geographical regions. Second, our analyses assumed that when stressful life events occurred in the same month as a depressive onset, that the relationship between these two occurrences was causal. We have previously shown, in two separate analyses (7, 35), that when

both are reported in a single month, the stressful life event—in nearly all instances—precedes the depressive onset (7, 35). More generally, we have also shown in this sample—using a co-twin control design—that the relationship between stressful life events and onset of major depression is mostly causal (8). Third, we examined only depressive onsets in the month of event occurrence. However, previous analyses in this sample have suggested that nearly all of the impact of stressful life events on risk of a depressive onset is contained in that first month (7, 35). Fourth, we did not measure the level of subjective distress in response to the stressful life events in our sample. It could be that such measures would further clarify gender differences in the relationship between stressful life events and risk for major depression. Fifth, we cannot rule out the possibility that our results were influenced not by gender differences in the actual occurrence of stressful life events or depressive episodes but by gender differences in the recall and reporting of these events. However, we have shown (36) that the genders do not, in this sample, differ in long-term reliability in reporting lifetime major depression. Sixth, we were unable, in our analyses of same-sex twin pairs, to correct for the correlated observations in twins. Our own experience, simulations (unpublished 2000 study of Gardner et al.), and the work of others (37) suggest that with sample sizes as large as those examined here, significant biases in estimation are unlikely unless the twin correlations are high. Twin correlations for month of occurrence of a depressive onset in this sample were, however, quite low (kappa=0.01) (7).

Received May 24, 2000; revision received Sept. 29, 2000; accepted Nov. 17, 2000. From the Departments of Psychiatry and Human Genetics, Medical College of Virginia, Virginia Commonwealth University, Richmond; and the Virginia Institute for Psychiatric and Behavioral Genetics. Address reprint requests to Dr. Kendler, Virginia Institute for Psychiatric and Behavioral Genetics, P.O. Box 980126, Richmond, VA 23298-0126.

Supported by grants from NIMH (MH-49492), the National Institute on Alcohol Abuse and Alcoholism (AA-09095), and a Research Scientist Award (MH-01277) to Dr. Kendler. The Mid-Atlantic Twin Registry, directed by Drs. L. Corey and L. Murrelle, has received support from NIH, the Carman Trust, and the W.M. Keck, John Templeton, and Robert Wood Johnson Foundations.

The authors acknowledge the contributions of the Virginia Twin Registry, now part of the Mid-Atlantic Twin Registry, in ascertainment of subjects for this study and Charles O. Gardner, Ph.D., who provided statistical advice.

References

- Boyd JH, Weissman MM: Epidemiology of affective disorders: a reexamination and future directions. Arch Gen Psychiatry 1981; 38:1039–1046
- 2. Weissman MM, Bruce ML, Leaf PJ, Florio LP, Holzer C: Affective disorders, in Psychiatric Disorders in America: The Epidemiologic Catchment Area Study. Edited by Robins LN, Regier DA. New York, Free Press, 1991, pp 53–80
- Kessler RC, McGonagle KA, Swartz M, Blazer DG, Nelson CB: Sex and depression in the National Comorbidity Survey, I: lifetime prevalence, chronicity and recurrence. J Affect Disord 1993; 29:85–96

- 4. Thoits PA: Dimensions of life events that influence psychological distress: an evaluation and synthesis of the literature, in Psychosocial Stress: Trends in Theory and Research. Edited by Kaplan HB. New York, Academic Press, 1983, pp 33–102
- Brown GW, Harris TO (eds): Life Events and Illness. New York, Guilford Press, 1989
- Kessler RC: The effects of stressful life events on depression. Annu Rev Psychol 1997; 48:191–214
- Kendler KS, Karkowski L, Prescott CA: Stressful life events and major depression: risk period, long-term contextual threat and diagnostic specificity. J Nerv Ment Dis 1998; 186:661–669
- Kendler KS, Karkowski LM, Prescott CA: Causal relationship between stressful life events and the onset of major depression. Am J Psychiatry 1999; 156:837–841
- Brown GW, Birley JLT: Crises and life changes and the onset of schizophrenia. J Health Soc Behav 1968; 9:203–214
- Bebbington PE, Tennant C, Hurry J: Adversity in groups with an increased risk of minor affective disorder. Br J Psychiatry 1991; 158:33–48
- Turner RJ, Avison WR: Gender and depression: assessing exposure and vulnerability to life events in a chronically strained population. J Nerv Ment Dis 1989; 177:443–455
- Newcomb MD, Huba GJ, Bentler PM: A multidimensional assessment of stressful life events among adolescents: derivation and correlates. J Health Soc Behav 1981; 22:400–415
- Wagner BM, Compas BE: Gender, instrumentality, and expressivity: moderators of the relation between stress and psychological symptoms during adolescence. Am J Community Psychol 1990; 18:383–406
- Perris H: Life events and depression, part 1: effect of sex, age and civil status. J Affect Disord 1984; 7:11–24
- Wilhelm K, Parker G: Sex differences in depressiogenic risk factors and coping strategies in a socially homogeneous group. Acta Psychiatr Scand 1993; 88:205–211
- Uhlenhuth EH, Paykel ES: Symptom intensity and life events.
 Arch Gen Psychiatry 1973; 28:473–477
- Uhlenhuth EH, Lipmann RS, Balter MB, Stern M: Symptom intensity and life stress in the city. Arch Gen Psychiatry 1974; 31: 759–764
- Kessler RC, McLeod JD: Sex differences in vulnerability to undesirable life events. Am Sociol Rev 1984; 49:620–631
- Nolen-Hoeksema S: Sex Differences in Depression. Palo Alto, Calif, Stanford University Press, 1990
- Bruce ML, Kim KM: Differences in the effects of divorce on major depression in men and women. Am J Psychiatry 1992; 149: 914–917
- 21. Nazroo JY, Edwards AC, Brown GW: Gender differences in the onset of depression following a shared life event: a study of couples. Psychol Med 1997; 27:9–19
- Van Os J, Jones PB: Early risk factors and adult person-environment relationships in affective disorder. Psychol Med 1999; 29: 1055–1067
- 23. Zimmermann-Tansella C, Donini S, Lattanzi M, Siciliani O, Turrina C, Wilkinson G: Life events, social problems and physical health status as predictors of emotional distress in men and women in a community setting. Psychol Med 1991; 21:505–513
- Leadbeater BJ, Kuperminc GP, Blatt S, Hertzog C: A multivariate model of gender differences in adolescents' internalizing and externalizing problems. Dev Psychol 1999; 35:1268–1282
- Kendler KS, Prescott CA: A population-based twin study of lifetime major depression in men and women. Arch Gen Psychiatry 1999; 56:39–44
- Spitzer RL, Williams JBW: Structured Clinical Interview for DSM-III-R (SCID). New York, New York State Psychiatric Institute, Biometrics Research, 1985
- 27. Kessler RC, McLeod JD, Wethington E: The costs of caring: a perspective on the relationship between sex and psychological

- distress, in Social Support: Theory, Research and Application. Edited by Sarason IG, Sarason BR. The Hague, Martinus Nijhoff, 1985, pp 491–506
- 28. Hosmer DW, Lemeshow S: Applied Logistic Regression. New York, John Wiley & Sons, 1989
- 29. SAS Language Reference, version 6. Cary, NC, SAS Institute, 1990
- 30. Maccoby EE: The Two Sexes: Growing Up Apart, Coming Together. London, Belknap Press (Harvard University Press), 1998
- 31. Zisook S, Downs NS: Death, dying, and bereavement, in Comprehensive Textbook of Psychiatry, 7th ed, vol 2. Edited by Sadock BJ, Kaplan VA. Philadelphia, Lippincott Williams & Wilkins, 2000, pp 1963–1981
- 32. Eagly A: Sex Differences in Social Behavior: A Social Role Interpretation. Hillsdale, NJ, Lawrence Erlbaum Associates, 1987

- 33. Swap WC, Rubin JZ: A measurement of interpersonal orientation. J Pers Soc Psychol 1983; 44:208–219
- 34. Gore S, Aseltine RH Jr, Colten ME: Gender, social-relational involvement, and depression. J Res Adolesc 1993; 3:101–125
- 35. Kendler KS, Kessler RC, Walters EE, MacLean C, Neale MC, Heath AC, Eaves LJ: Stressful life events, genetic liability, and onset of an episode of major depression in women. Am J Psychiatry 1995; 152:833–842
- 36. Kendler KS, Gardner CO, Prescott CA: Are there sex differences in the reliability of a lifetime history of major depression and its predictors? Psychol Med (in press)
- 37. Fitzmaurice GM: A caveat concerning independence estimating equations with multivariate binary data. Biometrics 1995; 51:309–317

593