Childhood Parental Loss and Adult Psychopathology in Women
A Twin Study Perspective
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- We examine the relationship between parental loss prior to age 17 years and adult psychopathology in 1018 pairs of female twins from a population-based registry. The relationship between loss and adult psychopathology varied as a function of the kind of loss (death vs separation), the parent involved, and the form of psychopathology. Increased risk for major depression and generalized anxiety disorder was associated with parental separation but not parental death and with separation from either mother or father. Panic disorder was associated with parental death and maternal, but not paternal, separation. Increased risk for phobia was associated with parental death and not parental separation. Risk for eating disorder was unrelated to the experience of parental loss. A model that includes parental loss as a form of "specified" family environment shows that, if it is truly an environmental risk factor for adult psychopathologic conditions, it can account for between 1.5% and 5.1% of the total variance in liability to these disorders and is responsible for between 7.0% and 20.5% of the tendency for these disorders to aggregate in siblings. (Arch Gen Psychiatry. 1992;49:109-116)

The loss of a parent in childhood, due either to death or separation, has long been considered an important risk factor for adult psychopathologic conditions. Psychoanalytic theorists have postulated that depression often arises as a result of a loss in adulthood that reactivates the trauma associated with childhood loss. Attachment theory posits an instinctive pattern of attachment behavior in infancy and childhood, the disruption of which can predispose to a variety of psychiatric disorders in adulthood. While early empirical investigations of the relationship between childhood parental loss and adult psychopathologic conditions were plagued by methodologic problems, the last two decades have seen an increasingly large and sophisticated body of work in this area, including both clinical and epidemiologic samples.

Most previous studies have focused on the relationship between early parental loss and depression in adulthood and have suggested that while separation from parents due to factors such as divorce or parental illness has a substantial and consistent relationship with depression, the effect of parental death is far less consistent and robust. The relationship between parental loss and antisocial personality and behavior has also been examined extensively.

Far fewer studies have examined the impact of early parental loss on the risk for other major adult psychiatric disorders. Four small clinical and two epidemiologic studies suggest a relationship between premature parental loss and anxiety disorders. Although psychoanalytic theory predicts that the impact of loss should be relatively specific to major depression, few studies have actually compared the relationship between parental loss and different major categories of psychiatric illness. In one such study, Tennant et al conclude that the impact of loss is greater on depression than on "anxiety states."

A GENETIC EPIDEMIOLOGIC PERSPECTIVE ON EARLY PARENTAL LOSS

One of the most consistent findings for all major psychiatric disorders has been their tendency to aggregate in families. Based on these results, psychiatric geneticists have attempted to quantify and uncover the genetic foundations of psychiatric illness. With a few notable exceptions, they have not been interested in environmental sources of familial resemblance. Therefore, they have usually been content to place all such environmental risk factors into a single latent unspecified variable, usually termed "common," "shared," or "familial" environment. By contrast, epidemiologists, who have more interest and expertise in measuring environmental risk factors, have usually paid little attention to the phenomenon of familial aggregation even if the risk factors they deal with, such as parental loss in childhood, have consistently been shown to have a strong influence on adult psychopathologic outcomes.
as parental loss, are themselves obviously familial.

If exposure to an environmental event increases risk for a psychiatric disorder and exposure to that event is correlated in relatives, then the disorder will aggregate in relatives solely as a result of the impact of the familial risk factor. The stronger the risk factor and the more familial it is, the greater will be the degree of familial aggregation of the disorder that it will cause.

Association studies in human genetics seek to "dissect out," from a background genetic effect, the impact on disease risk of a single, identifiable, genetic allele. In a parallel fashion, it is possible to move from inferring the impact of the family environment from correlational data to measuring specified aspects of the family environment. Just as the power to discern genetic effects increases markedly when individual genes can be identified, so environmental risk factors that are undetectable with realistic sample sizes as part of "background" familial environmen- tation, when they are specified, be easily detected, and their effect size estimated.

GOALS

From an epidemiologic perspective, we seek in this article to address the following questions: (1) What is the impact of early parental loss on risk for adult psychopathology in women and does the impact differ as a function of the kind of psychopathologic condition considered? (2) Does the impact differ as a function of the kind of loss (death vs separation) or the parent involved?

From a genetic epidemiologic perspective, we seek to answer the following questions: (1) Can the impact of early parental loss, modeled as "specified" family environment, on risk for adult psychopathologic condition be detected even when traditional twin models fail to detect any familial environmental effect? (2) What proportion of variance in liability to adult psychiatric disorders is accounted for by early parental loss? (3) What proportion of the familial resemblance for adult psychiatric disorder in siblings is due to their correlated exposure to early parental loss?

METHODS

Sample

As outlined in detail elsewhere, data for this report come from an ongoing study of genetic and environmental risk factors for common psychiatric disorders in white female twin pairs from the Virginia Twin Registry, a population-based registry formed from a systematic review of all birth records in the Commonwealth of Virginia. Twin pairs were eligible for this study if both members had previously responded to a mailed questionnaire, which had an individual response rate of 64%. Of the 1176 twin pairs who met these criteria, we proceeded in personally interviewing 92.0% of these twins, including both members of 1033 pairs. Of the completed interviews, 89.3% were performed face to face and 10.7% were performed by telephone. No differences were found in the rates of the disorders for those interviewed face to face vs by telephone. The mean (±SD) age of the sample at interview was 50.1 ± 7.6 years and ranged from 17 to 55 years. Zygosity was determined by self-report measures, photographs and, when necessary, DNA analysis using eight highly polymorphic probes. The final zygosity diagnosis yielded 590 monozygotic (MZ) twin pairs, 440 dizygotic (DZ) twin pairs, and three pairs of uncertain zygosity.

Measures and Interviewers

Lifetime psychiatric illness was diagnosed using an adapted version of the Structured Clinical Interview for DSM-III-R Diagnosis for major depression, generalized anxiety disorder, panic disorder, and eating disorders (anorexia nervosa and bulimia nervosa) and an adapted version of the Diagnostic Interview Schedule for phobia. All interviewers, who underwent extensive and ongoing training during the field study, had a minimum of a master's degree in psychology or social work or a bachelor's degree and at least 2 years of clinical experience. The same inter- viewer never interviewed both members of a twin pair.

Diagnostic Review

For phobia, diagnosis was based on the presence of an unreasonable fear and the assessment by the interviewer that this fear produced some objective interference in the respondent's life. For all other disorders, final project diagnoses were based on a blind review by one of us (K.S.K.), an experienced psychiatrist diagnostician, using DSM-III-R criteria. The one exception to this was for generalized anxiety disorder, where we adopted the DSM-III convention of a minimum 1-month duration of illness in preference to the DSM-III-R convention of 6 months. In this article, we report only those diagnoses assigned at a probable or definite level, meaning that on review, these cases were considered to meet, with little uncertainty, the relevant diagnostic criteria. No corrections for comorbidity were used in these analyses, so that an individual with more than one disorder was considered affected for each disorder for which she met criteria. Of the twins meeting criteria for phobia, 41% met criteria for situational phobia, 38% met criteria for social phobia, 36% met criteria for animal phobia, and 29% met criteria for agoraphobia. These figures sum to more than 100% because about one-third of the twins diagnosed as having a phobia met criteria for more than one subtype.

Definition of Parental Loss

Premature parental loss, defined as the twin living apart from one or both of her natural parents for at least 1 year prior to her 17th birthday, was divided into those due to parental death and those due to separation of the parent from the twins for other reasons (terming "separation"). In our sample, 92% of these separations were associated with parental divorce. In the small number of cases (n = 7) where separation preceded death, both events were counted. The age of the twin at parental death or at the first separation was recorded. For this article, we restricted our sample to those twin pairs where both members had had the same experience of either continued parental contact or loss (n = 1018).

Statistical Analysis

Two different analytic methods were used in this report: logistic regression and structural equation model fitting.

Regression and Relative Risk Analyses.—In the logistic regression analyses, performed using the LOGISTIC procedure in SAS, the twin-family was the unit of analysis and the dependent variable was dichotomous: (1) neither twin affected, (2) one twin affected, and (3) both twins affected. The parallel lines assumption for ordinal logistic regression was tested for all 15 analyses conducted, and it was rejected at the 5% level only twice, a result not different from chance expectation. The age of the twin at interview and the socioeconomic status of the parents (as indexed by years of education and occupational status) significantly predicted premature parental loss and were therefore included as control variables. We first examined the effect of any loss on adult psychopathology and then, in a single analysis, the effect of any death and any separation. Then, in a separate analysis, we examined the effect of maternal and paternal separation, controlling for the effect of parental death, the number of which was too small to subdivide meaningfully into maternal and paternal. Too small a proportion of our sample experienced more than one kind of parental separation for us to meaningfully examine interactions between kinds of losses in predicting adult psychopathologic conditions. In addition, the relative risks for the impact of parental loss, controlling for the effect of age at interview and parental social class, were
calculated treating the 2036 members of the twin pairs as individuals. Because observations from members of a twin pair are not independent and significance levels are already available from the regression analysis, no attempt was made to calculate significance levels for the relative risks.

In examining the impact of age at loss on risk for adult psychopathological conditions, analyses were restricted to those twin families that reported a loss. We examined both the quadratic and linear impact of age at loss on risk for adult psychopathological conditions, but the quadratic effect was rarely significant and did not add substantially to the interpretation of the available results. When there were differences in the reported age of the twins at the time of loss, the mean of the reports of the two twins was used.

**Structural Equation Modeling.**—Structural equation modeling applied to psychopathology is based on a "liability-threshold" model that assumes that underlying the observed dichotomy of "unaffected/affected," there exists a continuous, normally distributed latent liability.** Individuals whose liability exceeds a certain threshold are assumed to manifest the disorder. Although this model classically assumes a very large number of genetic and environmental factors of small effect, in fact a normal distribution of liability can be closely approximated by a small number of factors of moderate-sized effect.

As we have outlined previously, in a traditional twin model, the goal is to divide the sources of variance in liability to a disorder into that proportion accounted for by genetic, common, or familial environmental and individual specific environmental factors. All of these factors, however, are latent and not directly observed. The model used in this report differs from the traditional twin model in that, in addition to the standard latent common environment component, the models also include a specified common environment: childhood parental loss.

The full model used is illustrated in Fig 1. As is traditional for path models, observed variables are placed in boxes and latent variables are placed in circles. Age at interview is included because it significantly predicts the probability of premature parental loss. Discounting the effects of age, this model postulates that twin resemblance results from three classes of factors: latent additive genetic factors (A), latent common environment (C), and observed common environment (parental death and separation).

Tetrachoric and point-biserial correlations for the variables of interest (psychiatric diagnosis, age at interview, separation history) were calculated separately for MZ and DZ twins with the use of TRELIS. Models were fit to these correlation matrices by LISREL. Our goal was to obtain the best possible explanation of the observed data with the fewest possible parameters. We fit an extensive series of models (details available on request) and chose the model that minimized, or made most negative, the value of Akaike's information criterion (AIC), a statistic that equals the $\chi^2$ fit of the model minus twice the $df$, and reflects both the model's goodness of fit and parsimony. The parameter estimates of the best-fitting model were then used to calculate the proportion of the correlation in liability in DZ twins that can be explained as a result of their perfectly correlated experience with or without parental separation.

**RESULTS**

Number of Twin Families With Separation

As seen in Fig 2, of the total of 1018 twin pairs in which both twins agreed on the presence or absence of parental loss up through age 16 years, 178 or 17.5% experienced parental loss. A total of 62 (6.1%) twin pairs experienced parental death while 123 (12.1%) pairs experienced separation. In three cases, all fathers, the twins agreed that the death was a probable or definite suicide. Both death and separation occurred about four times as frequently in fathers as in mothers.
Table 1.—The Impact of Parental Loss on Risks for Adult Psychopathology*

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Any Loss</th>
<th>Death</th>
<th>Separation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Logistic</td>
<td>Relative</td>
<td>Logistic</td>
</tr>
<tr>
<td></td>
<td>Regression</td>
<td>Risk</td>
<td>Regression</td>
</tr>
<tr>
<td>Major depression</td>
<td>+0.40†</td>
<td>1.27</td>
<td>-0.17</td>
</tr>
<tr>
<td>Generalized anxiety disorder</td>
<td>+0.57‡</td>
<td>1.43</td>
<td>+0.11</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>+0.73§</td>
<td>2.08</td>
<td>+0.72†</td>
</tr>
<tr>
<td>Phobia</td>
<td>+0.35†</td>
<td>1.21</td>
<td>+0.59†</td>
</tr>
<tr>
<td>Eating disorder</td>
<td>+0.01</td>
<td>1.06</td>
<td>-0.78</td>
</tr>
</tbody>
</table>

*Controlling for age at interview and parental social class.
†P<.05.
‡P<.001.
§P<.01.
∥P<.10.

Table 2.—The Impact of Maternal vs Paternal Separation on the Risk for Adult Psychopathology in Disorders Significantly Predicted by Parental Separation*

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Maternal Separation</th>
<th>Paternal Separation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Logistic Regression</td>
<td>Relative Risk</td>
</tr>
<tr>
<td>Major depression</td>
<td>+0.57</td>
<td>1.53</td>
</tr>
<tr>
<td>Generalized anxiety disorder</td>
<td>+1.04†</td>
<td>2.01</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>+1.06‡</td>
<td>3.38</td>
</tr>
</tbody>
</table>

*Controlling for age at interview and parental social class.
†P<.01.
‡P<.05.

Separation and Risk for Adult Psychopathology

The impact of early parental loss on risk for adult psychopathology, as assessed by logistic regression controlling for age at interview and parental social class, is seen in Table 1. The relationship between premature parental loss and risk is strongest in panic disorder, followed by generalized anxiety disorder, major depression, phobia, and eating disorders.

The effects of death and separation on risk for adult psychopathologic conditions are also seen in Table 1. Premature parental death significantly predicts risk only for panic disorder and phobia. By contrast, separation in childhood and adolescence significantly predicts risk for major depression, generalized anxiety disorder, and panic disorder.

The impact of separation from mother vs father is seen in Table 2. Depression is about equally associated with maternal and paternal separation. By contrast, for generalized anxiety disorder and particularly for panic disorder, separation from mother is a stronger predictor of risk than separation from father.

Age at Separation and Risk for Adult Psychopathology

We examined the impact of age at any loss and for death and separation on risk for major depression, generalized anxiety disorder, panic disorder, and phobia. Only one result of 12 was significant at the 5% level and three were significant at the 10% level. The only consistent pattern was seen for panic disorder, where age at any loss or loss due to death or separation were all negatively related to risk.

The Impact of Zygosity

Our twin families consisted of two potentially different populations: those with MZ and those with DZ twins. Controlling for age and parental social class, zygosity did not predict any parental loss or loss due to death or separation. Next we examined whether the impact of parental separation differed in families containing MZ vs DZ twins. No significant interaction was found in predicting any form of psychopathology between zygosity and any loss, death vs separation, or maternal vs paternal separation.

Table 3.—Results of Fitting Full Model Including Parental Loss as a Specified Family Environment to Major Depression*

<table>
<thead>
<tr>
<th>Parameters of Loss Model</th>
<th>Parameters of Genetic Model</th>
<th>Main</th>
<th>Miscellaneous</th>
<th>(\chi^2)</th>
<th>df</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A,C,E</td>
<td>D,S</td>
<td>Al, Corr</td>
<td>5.31</td>
<td>12</td>
<td>-18.69</td>
</tr>
<tr>
<td>2</td>
<td>A,E</td>
<td>D,S</td>
<td>Al, Corr</td>
<td>5.31</td>
<td>13</td>
<td>-20.69</td>
</tr>
<tr>
<td>3</td>
<td>C,E</td>
<td>D,S</td>
<td>Al, Corr</td>
<td>10.52</td>
<td>13</td>
<td>-15.48</td>
</tr>
<tr>
<td>4</td>
<td>A,E</td>
<td>S</td>
<td>Al, Corr</td>
<td>5.38</td>
<td>14</td>
<td>-22.62</td>
</tr>
<tr>
<td>5</td>
<td>A,E</td>
<td>D</td>
<td>Al, Corr</td>
<td>13.46</td>
<td>14</td>
<td>-14.54</td>
</tr>
<tr>
<td>6</td>
<td>A,E</td>
<td>S</td>
<td>Corr</td>
<td>7.18</td>
<td>15</td>
<td>-22.82</td>
</tr>
<tr>
<td>7</td>
<td>A,E</td>
<td>S</td>
<td></td>
<td>7.85</td>
<td>18</td>
<td>-22.15</td>
</tr>
</tbody>
</table>

*AIC indicates information criterion of Akaike [3]; Al, age at interview; Corr, correlations between parental death and parental separation, parental death and age at interview, and parental separation and age at interview. A, additive genetic effects; C, common or familial environmental effects; D, individual specific environmental effects; S, effect of parental death; and S, the effect of parental separation.

†Best-fitting model.

Twin Model Fitting With Loss as 'Specified' Familial Environment for Major Depression

We present, in detail, results of twin model fitting with parental death and separation as specified family environment for major depression (Table 3). Results of standard model fitting for this disorder in our entire sample have been presented elsewhere. In model fitting, our goal is to find the most parsimonious model that provides a good explanation of the observed data, which is herein operationalized as the model that produces the most negative value of the AIC. Model 1, the full model depicted in Fig 1, fit well (\(\chi^2\) goodness of fit = 5.31, df = 12, AIC = -18.7) and can be usefully divided into a standard twin model (upper half of figure) and a "loss model" (lower half of figure). We first determine the best-fitting "standard" twin model. While eliminating the latent common environment (model 2) resulted in an
improvement in the AIC ($\chi^2 = 5.31, \text{df} = 13, \text{AIC} = -20.7$), eliminating additive genetic effects (model 3) resulted in a deterioration of fit ($\chi^2 = 10.52, \text{df} = 13, \text{AIC} = -15.5$). Given that the best-fitting genetic model assumes additive genetic effects (A) and individual specific environment (E), we then turn to the loss model. While setting to zero the path from parental death to depression (model 4) results in a further improvement in the AIC ($\chi^2 = 5.38, \text{df} = 14, \text{AIC} = -22.6$), doing this with the path from parental separation to depression (model 5) results in a substantial deterioration in fit ($\chi^2 = 14.16, \text{df} = 14, \text{AIC} = -14.5$). Having set to zero the effect of parental death, we then set the effect of age (model 6) and all the correlations among age, death, and separation (model 7) to zero, noting that each of these steps results in further improvement in the AIC. The results of best-fitting model, model 7, which includes only additive genetic effects, individual specific environmental and parental separation ($\chi^2 = 7.85, \text{df} = 18, \text{AIC} = -28.2$), are seen in Fig. 3.

Parental Loss and Familial Aggregation of Psychiatric Disorders

We proceeded to fit a similar series of models to the other psychiatric disorders. As with the regression analyses, we found evidence for a significant effect of at least one form of parental loss for every disorder except eating disorders. The proportion of total variance in liability to each of these disorders accounted for by parental loss in the best-fit model is seen in Table 4. As with the regression models, twin model fitting with specified family environment found that only separation was significant for generalized anxiety disorder and alcoholism, only parental death was significant for phobia, and both death and separation were significant for panic disorder. The impact of parental loss was greatest for panic disorder (4.9% of the total variance in liability) and smallest for major depression (1.6%). In interpreting these figures, it is important to recall that they refer to the total population and are a function both of the frequency and magnitude of impact of parental separation on liability to illness.

It was also possible to calculate what proportion of the correlation in liability in DZ twins could be explained by the fact that in this sample, they always shared their experience of continuous parental care vs. loss. Again, the impact of parental loss was greatest for panic disorder, where it could account for 19.5% of the tendency for the disorder to aggregate in siblings. The impact of parental loss was least for major depression, where it could account for 7.1% of the correlation of liability to depression in siblings.

COMMENTS

The goal of this article was to clarify from an epidemiologic and genetic-epidemiologic perspective the impact of parental loss on adult psychopathology in women. We will review each of our major results in turn.

The Impact of Premature Parental Loss

Controlling for the effect of age at interview and parental social class, parental loss prior to age 17 years was significantly related to five of the six major psychiatric disorders examined. Only the risk for eating disorders was unaffected by premature parental loss. Parental loss was not, in our sample, specific in its effect, being associated with an increase in risk for depression, generalized anxiety disorder, panic disorder, and phobias.

However, the effect on children of parental loss due to death vs. due to separation is likely to be qualitatively different. Consistent with most previous epidemiologic and clinical studies, the risk for depression in our sample was significantly related to a history of parental separation but not of parental death. The same pattern was observed for generalized anxiety disorder, which is in accord with the findings from several small sample clinical studies, but not with the one large-sample epidemiologic study of this question. Compatible with the results of Tweed et al., we found that panic disorder was significantly and strongly associated with both parental death and separation, while phobias were associated with parental death only. Our results do not support the findings of Tennant et al. that childhood parental loss is more strongly related to depression than to anxiety disorders.

SEPARATION FROM MOTHER VS. FATHER

Much work on the impact of parental separation has focused exclusively on mothers, usually assuming that separation would be more pathogenic than paternal separation. We found for depression that maternal and paternal separation were associated with the same increase in risk, although only the latter, because of larger numbers, reached statistical significance. Previous studies have disagreed about the relative importance of separation from mother vs. father in the pathogenesis of depression.

The pattern seen in depression was not the same as that
found for generalized anxiety or panic disorder, where maternal separation was much more strongly related to disease risk than was paternal separation. These results disagree with the findings of Tennant et al. from a general population sample where maternal and paternal loss had similar effects on the risk for anxiety states.

**Panic Disorder, Phobias, and Separation Anxiety**

Considerable evidence exists for a relationship between separation anxiety in childhood and adult panic disorder and phobia. It is tempting to speculate that the difference in the pattern of results for panic and phobia vs depression might result from certain kinds of losses (e.g., parental death vs separation or maternal vs paternal separation) predisposing to childhood separation anxiety and hence to adult panic disorder and phobia. Along these lines, it is of interest to note that while any parental separation is not significantly related to risk for phobia in our sample, the risk for phobia is moderately increased by maternal ($P<.10$) but not at all by paternal separation. Unfortunately, further information is not currently available in our data set to address this interesting hypothesis.

**Early Parental Loss From a Genetic Epidemiologic Perspective**

Parental loss in childhood and adolescence is an attractive variable for genetic epidemiologists because it is a risk factor the exposure to which is perfectly correlated in siblings who are reared together. By exclusion the small number of families in which twins had different rearing experiences, it was easy to create a data set in which parental loss could be conceptualized as a specified form of family environment.

Power analyses have demonstrated that for a trait with moderate heritability, the detection, by the traditional methods of twin modeling, of familial environmental variance that accounts for even 10% to 15% of the overall variance requires sample sizes of well over 1000 twin pairs. By these traditional methods, we could find, in our sample, no evidence for family environment in the etiology of major depression. However, when we moved from treating family environment as an unspecified, latent variable, to a specified, measured variable, in the form of parental loss, our statistical power increased dramatically. We were able to detect the impact of parental loss due to separation on the liability to major depression, even though that loss accounted for less than 2% of the total variance. These results underline the great gain in analytic power that occurs as genetic epidemiologic models for psychiatric disorders move from treating the environment as an unmeasured latent “black box” to considering it as an array of specific measurable environmental variables.

A genetic-epidemiologic perspective on parental loss has at least two advantages over the more traditional epidemiologic approach. First, it allows the quantification of the impact of parental loss on liability to illness relative to that of other major classes of risk factors. Thus, for depression, we can estimate that the genetic contribution to major depression is, in the general population of female twins, approximately 25 times as important as is parental loss. Second, the genetic-epidemiologic approach allows us to view parental loss as an environmental risk factor that contributes to familial aggregation. While contributing relatively modestly to total variance, our results suggest that parental loss contributes substantially to the aggregation within sibships of generalized anxiety disorder, panic disorder, and phobias.

**Loss and Adult Psychopathology: Correlation vs Causation**

We have in this article demonstrated an association between early parental loss and adult psychopathologic conditions. However, correlation need not imply causation. The psychoanalytic and attachment theories, which both posit that the impact of parental loss occurs from the enduring psychological scar resulting directly from the experience of loss, are not the only plausible hypotheses for the association between parental loss and adult psychopathologic conditions. The impact of parental separation may be mediated not by the loss of the parent, but rather by the exposure to the parental discord that usually precedes it or the poor parental care that often follows it. Alternatively, the impact of parental loss may be mediated by the social and economic sequelae of family disruption. Parental divorce is associated with lower educational attainment and earlier age at marriage for daughters. The apparent impact of parental loss may be mediated entirely by genetic factors that both predispose to poor marital adjustment or poor health in the parental generation and to liability to psychiatric disorders in the offspring generation. The impact of parental separation may be mediated not by the direct impact of parental discord on the developing child but rather by the cross-generational cultural transmission of marital instability, which in turn is a major risk factor for adult psychopathologic conditions.

**Limitations and Strengths of the Sample**

Results presented herein should be interpreted in the context of the several potentially important strengths and limitations. Two important methodologic strength warrant mention. First, as an epidemiologic sample, our results are not influenced by help-seeking behavior. This is particularly important because of evidence that parental loss may directly increase the probability of an individual seeking treatment for psychiatric conditions. Second, by accepting into our sample only twin pairs where both concurred in reporting the presence or absence of parental loss, we markedly diminish the possible impact of both unreliability and bias in the retrospective reporting of parental loss (e.g., an individual with a history of depression being more likely to remember and report parental loss than one without such a history).

Four potential limitations should also be kept in mind in considering the results presented herein. First, the sample considered is entirely twins who are female and white. Given evidence that parental loss may impact differently as a function of sex and race, results presented herein should not be assumed to extrapolate to nonwhite and/or mixed sex populations. It is also possible that the impact of parental separation might differ in twins and in singletons.

Second, while based on a complete search of birth certificates, our final study sample is unlikely to be perfectly representative of the entire twin population. Twins who moved out of state or did not return earlier questionnaires were unlikely to be included in our sample.

Third, the results presented herein are, in at least two important ways, incomplete. Substantial evidence suggests that parental separation may be best considered an...
index of other familial environmental risk factors, especially marital discord and poor quality of rearing. If this is correct, then direct measures of these underlying risk factors, which are available in this data set, may show yet stronger effects on adult psychopathologic conditions. We have also made no attempt to trace the “path” by which parental loss leads to adult psychopathologic conditions. Information is available for a number of these potential intervening variables (eg, social class and educational attainment of twin, age at first marriage, history of divorce, and marital quality for the twin).

Finally, the validity of our results using parental loss as a specified form of familial environment is dependent on the validity of our model that assumes, as have nearly all the previous studies in this area, that childhood parental loss is truly “environmental” and causally related to adult psychopathologic conditions. In particular, our model does not incorporate parental psychopathology that might both increase the risk for parental loss and, by genetic and/or cultural transmission, increase the risk for psychiatric disorders in offspring. If this is the case, then the results of this report will need to be reinterpreted, as parental loss may be more a reflection of parental genotype than a true environmental risk factor for the offspring. We are currently interviewing all living and cooperative parents of our twins and therefore will, in the future, in the setting of a twin-family design, be able to address these important issues regarding the relationship between parental separation and psychopathology.

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