Article

Toward a Comprehensive Developmental Model for Major Depression in Men

Kenneth S. Kendler, M.D.

Charles O. Gardner, Ph.D.

Carol A. Prescott, Ph.D.

Objective: The multiple risk factors for major depression are interrelated through poorly understood developmental pathways. In 2002, the authors presented a developmental model for major depression in women. Based on similar methods, they here present an analogous model for men.

Method: Using data from 2,935 adult male twins, interviewed twice over a 2–4-year period, the authors constructed, by means of structural equation modeling, an integrated etiologic model for major depression that predicts depressive episodes over 1 year from 18 risk factors conceptualized as five developmental "tiers" reflecting childhood, early adolescence, late adolescence, adulthood, and the last year.

Results: The best-fitting model, including six correlations and 76 paths, provided a good fit to the data, explaining 49% of the variance in the liability to depressive episodes. The overall results, similar to those seen in women, suggest that the development of major depression results from the action and interaction of three broad pathways of internalizing symptoms, externalizing symptoms, and adversity. Childhood parental loss and low self-esteem were more potent variables in the model in men than in women. Genetic risks for major depression had a broader spectrum of action in men than in women. The pathway to major depression through externalizing symptoms was not more prominent in men than in women.

Conclusions: Major depression in men, as in women, is an etiologically complex disorder influenced by risk factors from multiple domains that act in developmental time. The similarities in etiologic pathways to major depression for men and women outweigh the modest differences.

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Major depression is a paradigmatic multifactorial disorder, where risk of illness is influenced by a range of factors including genetic liability, poor parenting, traumatic experiences, predisposing personality traits, early-onset anxiety disorder, poor self-esteem, low social support, substance misuse, marital difficulties, a prior history of major depression, and recent stressful life events and difficulties. The need to organize these diverse risk factors into an integrated etiologic model to elucidate developmental pathways has been long recognized (1). In 2002, we published such a preliminary model in female twins (2).

Numerous studies have examined sex differences in the prevalence and risk factors for major depression (3, 4). While higher rates in women are consistently reported, finding robust, replicable differences in risk factors for major depression in the two sexes has been more difficult. Furthermore, studies have typically compared only a small number of risk factors. We are unaware of prior attempts to compare comprehensive etiologic models for major depression in the two sexes.

This report has two goals. First, we describe a detailed developmental model for the etiology of major depression in men that was developed by using methods that parallel our prior efforts in women (2). Second, we compare the results of these etiologic models in women and men.

Method

Sample

We used data from a two-wave study of male-male and male-female pairs from the Virginia Twin Registry, formed by a search of all Virginia birth certificates since 1918. Twins were eligible if one or both members were successfully located, members of a multiple birth including at least one male, Caucasian, and born between 1940 and 1974 (5). Of 9,417 eligible individuals for the first wave (time 1), interviews were completed, typically by telephone, with 6,814 (72.4%). At least 1 year later, we recontacted the twins to schedule a second-wave interview (time 2). This interview was successfully completed, mostly face-to-face, with 5,629, or 82.6% of those eligible. Signed informed or verbal consent was, respectively, obtained prior to all face-to-face and telephone interviews. To assess test-retest reliability, 131 members of the male-male pairs were reinterviewed a mean of 4.4 months (SE=1.1) after their initial interview.

This report is based on 2,935 members of male-male pairs who completed both interviews: 1,197 complete pairs and 541 single twins whose co-twin did not complete both interviews. At the time 2 interview (1994–1998), the subjects had a mean age and years of education of 37.0 (SD=9.2) and 13.5 (SD=2.7), respectively. The interviewers were clinically trained. Each interview was reviewed twice for completeness and consistency. The two members of each twin pair were interviewed by different interviewers.

Outcome Variable

Our model predicted episodes of major depression in the year prior to the time 2 interview. Major depression was treated as a di-

chotomous variable, with the assumption of an underlying normal liability distribution. In the time 2 interview, twins were asked about the occurrence in the last year of 15 symptoms reflecting all DSM-III-R A criteria for major depression. They then aggregated these symptoms in time, reported the total number of episodes, and dated, to the month, the onset and offset of each episode. We examined the first reported episode meeting the criteria unless there were multiple episodes and the first episode began in the first 2 months of the year, in which case we took the next reported episode. The test-retest reliability for last-year major depression was good: kappa=0.74 (SE=0.08), tetrachoric r=0.96 (SE=0.03).

Model Variables

The variables examined in this study paralleled as closely as possible those used in our prior investigation of twins from female-female pairs (2). Exact replication was not possible because our four-wave study of female-female pairs contained variables not assessed in our male-male pairs. Also, we had personally interviewed parents of our female-female but not male-male pairs.

As previously (2), we examined 18 predictor variables organized into "tiers" roughly approximating five developmental periods: childhood (genetic risk, low parental warmth, childhood sexual abuse, and parental loss), early adolescence (neuroticism, low self-esteem, early-onset anxiety, and conduct disorder), late adolescence (low educational achievement, lifetime traumas, low social support, and substance misuse), adulthood (history of divorce and past history of major depression), and the last year (last-year marital problems, difficulties, and dependent and independent stressful life events). (The latter four of these tiers are conceptual rather than statistical entities as the final 15 variables in the model are simply consecutively ordered. The first four are distinct because they are interconnected by correlations—depicted by two-headed arrows in the figures—rather than partial regression coefficients—depicted by one-headed arrows.)

One of these 18 predictor variables, substance misuse, was latent and was constructed, by using a measurement model, from other observed variables. We here outline briefly each variable; for further details see our previous article (2).

Genetic risk. Genetic risk was assessed by a composite measure of the lifetime history of major depression in the co-twin (assessed at time 1 and time 2) and in the mother and father as assessed by the family history report of the two twins at time 2 according to the Family History Research Diagnostic Criteria (6). Parents were separately divided into three liability categories: history of major depression as reported by neither, one only, or both members of the twin pair. Co-twins were divided into three categories reflecting their report of a history of major depression at neither, one, or both of the personal interviews. To correct for varying base rates and degree of genetic relatedness in these relatives, we calculated the modified midrank score for the lifetime history of major depression and adjusted these scores to account for the varying genetic correlation with the proband twin (1.00 for monozygotic co-twins and 0.50 for dizygotic co-twins and parents). We then took the mean of the three scores of the co-twin, mother, and father.

Low parental warmth. This variable was assessed by using a modified version of the Parental Bonding Instrument (7). We took the mean of up to eight reports from a twin pair with each twin reporting on the level of warmth he received and he observed his twin receiving from both their mother and father. In our study of female-female twins, this variable was termed "disturbed family environment" because it included additional measures of family environment not available in our male-male sample and also included reports from the parents of the twins.

Childhood sexual abuse. This was determined from a single item in the time 1 interview: "Have you ever been sexually abused or molested?" If a positive response was given, the age at which this first occurred was recorded. In this report, childhood sexual abuse was considered present if the age given was prior to 16.

Parental loss. This binary measure was scored as 1 if the twin reported that one or more parents left the nuclear home through death, divorce, or parental separation prior to age 17.

Neuroticism. The short-scale (12-item) version from the revised Eysenck Personality Questionnaire (8) was used to obtain a neuroticism score at time 1. Because of its J-shaped distribution, we scored it as a five-level ordinal measure.

Self-esteem. The full Rosenberg self-esteem scale (9) was administered at time 1. It was reverse scored so that higher scores reflected lower self-esteem.

Early-onset anxiety disorder. This was a binary variable scored as 1 for subjects with an onset prior to age 18 of panic disorder, generalized anxiety disorder, or any form of phobia as assessed at the time 2 interview by using diagnostic criteria outlined previously (2).

Conduct disorder. We treated conduct disorder as an ordinal variable that reflected the number of DSM-IV conduct disorder criteria met prior to age 18 that were endorsed at time 1.

Years of education. Education level was treated as a continuous variable and was assessed at the time 1 interview. It was reverse scored to reflect low education.

Lifetime traumas. The number of traumas was reflected by the number of items reported at the time 1 interview that assessed exposure to combat, life-threatening accident, natural disaster, severe injury, physical assault, and being threatened with a weapon. The distribution was skewed, so it was treated as an ordinal variable.

Social support. Social support was assessed from the time 1 interview. We took the overall mean of 16 items reflecting the frequency of interpersonal contact, the degree of social integration, and the quality of the relationships with spouse, twin, children, parents, other relatives, and friends. This measure, which was scored to reflect lack of social support, was relatively symmetric and was treated as a continuous variable.

Substance misuse. This was assessed by using a measurement model derived from a lifetime diagnosis of DSM-III-R alcohol abuse or dependence assessed at time 1 or time 2, DSM-IV drug abuse or dependence assessed at time 2, and nicotine dependence as assessed by a score of ≥7 on the Fagerstrom Tolerance Questionnaire (10) collected at time 2.

Ever divorced. This binary measure was scored as 1 for men who reported a lifetime history of divorce or annulment at the time 2 interview.

Prior history of major depression. This was a binary measure reflecting the presence or absence of a lifetime history of DSM-III-R major depression, as reported at either the time 1 or time 2 interview, with an onset at least 8 years before the time 2 interview. This time period was chosen to parallel the time period between last-year and prior history of major depression used in our model with female twins (2).

Last-year marital problems. We constructed marital problems as a three-level ordinal variable using seven items assessing the level of marital satisfaction in the last year, obtained from the Social Interaction Scale (11), at the time 2 interview.

Last-year difficulties and dependent and independent stressful life events. We assessed these occurrences, using our stressful life event measures, in the time 2 interview. Each twin was systematically asked about the occurrence, at any time in the preceding 12 months, of 11 "personal" events and four classes of "network" events, each event being dated to the nearest month with high interrater reliability (12). The dependence of a stressful

life event, reflecting the probability that the respondent's own behavior contributed to the stressful life event, was rated on a 4-point scale. In these analyses, we dichotomized stressful life events into those clearly or probably independent versus those clearly or probably dependent.

For an individual with a reported onset of major depression in the year preceding his time 2 interview, we counted, separately, the numbers of dependent and independent life events occurring in that month and the 2 preceding months (12). For individuals reporting no depressive onset, a random 3-month window was used to assess the occurrence of stressful life events. The number of stressful life events was treated as an ordinal variable. Last-year difficulties reflected the sum of all stressful life events reported at other times during the year prior to the time 2 interview.

Statistical Methods

Model fitting was done by means of Mplus version 3 (13) because of its ability to combine categorical, ordinal, and continuous data. The fit function used was weighted least squares. To avoid loss of subjects due to missing information, our raw data were first put through multiple imputation by using IVEware (14, 15), which utilizes a multivariate sequential regression approach using linear regression for continuous variables, Poisson regression for count variables, and logistic regression for ordinal and binary variables (16). Five imputed data sets were created and then combined for analysis in a multigroup analysis in Mplus.

Our approach to model fitting was identical to that used previously (2) with one exception. Because of changes in the Mplus program, getting our model to converge required setting the thresholds rather than estimating them. We began with a fully saturated model and fixed to zero all paths with an associated z value of <1.96. Next, because of our large sample size, some paths remained significant that were too small to be meaningful. Therefore, our second step was to set all paths to zero with a value of <0.05, regardless of z value. All remaining paths in the model were statistically significant. This approach does result in the inclusion of paths in the model that have quite modest explanatory power.

We utilized three fit indices that reflect the success of the model in balancing explanatory power and parsimony: the Tucker-Lewis index (17), the comparative fit index (18), and the root mean square error of approximation (19). For the Tucker-Lewis index and comparative fit index, values between 0.90 and 0.95 are considered acceptable and ≥0.95 is considered good. For the root mean square error of approximation, good models have values of ≤0.05.

Results

Model Fitting

Of the 2,935 male twins who participated in the second interview wave, 179 (6.1%) reported a depressive episode meeting DSM-III-R criteria in the last year. The best-fit model predicting these episodes (fit to five replicates) produced a chi-square value of 2,242.4 with df=1,094, accounted for 48.7% of the variance in liability to last-year major depression, and produced the following fit indices: comparative fit index=0.948, Tucker-Lewis index=0.951, and root mean square error of approximation=0.019.

Parameter Estimates

Childhood risk factors. As seen in Figure 1, modest interfactor correlations were seen between the four childhood risk factors. Higher genetic risk for major depression was associated with a lower level of parental warmth and higher risks for childhood sexual abuse and childhood parental loss.

As seen in Figure 2, when the analysis controlled for all the other variables in the model, high genetic risk for major depression was uniquely predictive of nine "downstream variables": neuroticism, early-onset anxiety, conduct disorder, lifetime trauma, substance misuse, past history of major depression, last-year difficulties, independent stressful life events, and the probability of a depressive episode in the last year.

Low parental warmth uniquely predicted all four of the early adolescent risk factors, as well as lifetime trauma and low level of social support (Figure 1).

Childhood sexual abuse uniquely predicted a wide array of further variables: neuroticism, conduct disorder, other lifetime trauma, substance misuse, history of divorce, past history of major depression, and all four of the "last year" risk factors.

Childhood parental loss uniquely predicted all four of the early adolescent risk factors as well as low educational achievement, substance misuse, and dependent stressful life events.

Risk factors of early adolescence. Neuroticism had a strong relationship with low self-esteem and early-onset anxiety disorder. High levels of neuroticism also uniquely predicted conduct disorder, prior history of major depression, and last-year marital problems (Figure 1).

Low self-esteem uniquely predicted low educational attainment, low level of social support, marital problems, and both past history and last-year history of major depression.

Early-onset anxiety disorder increased the risk for conduct disorder, past history of major depression, and last-year difficulties.

Conduct disorder symptoms increased the risk for low educational attainment, lifetime traumas, low social support, and particularly strongly, substance use.

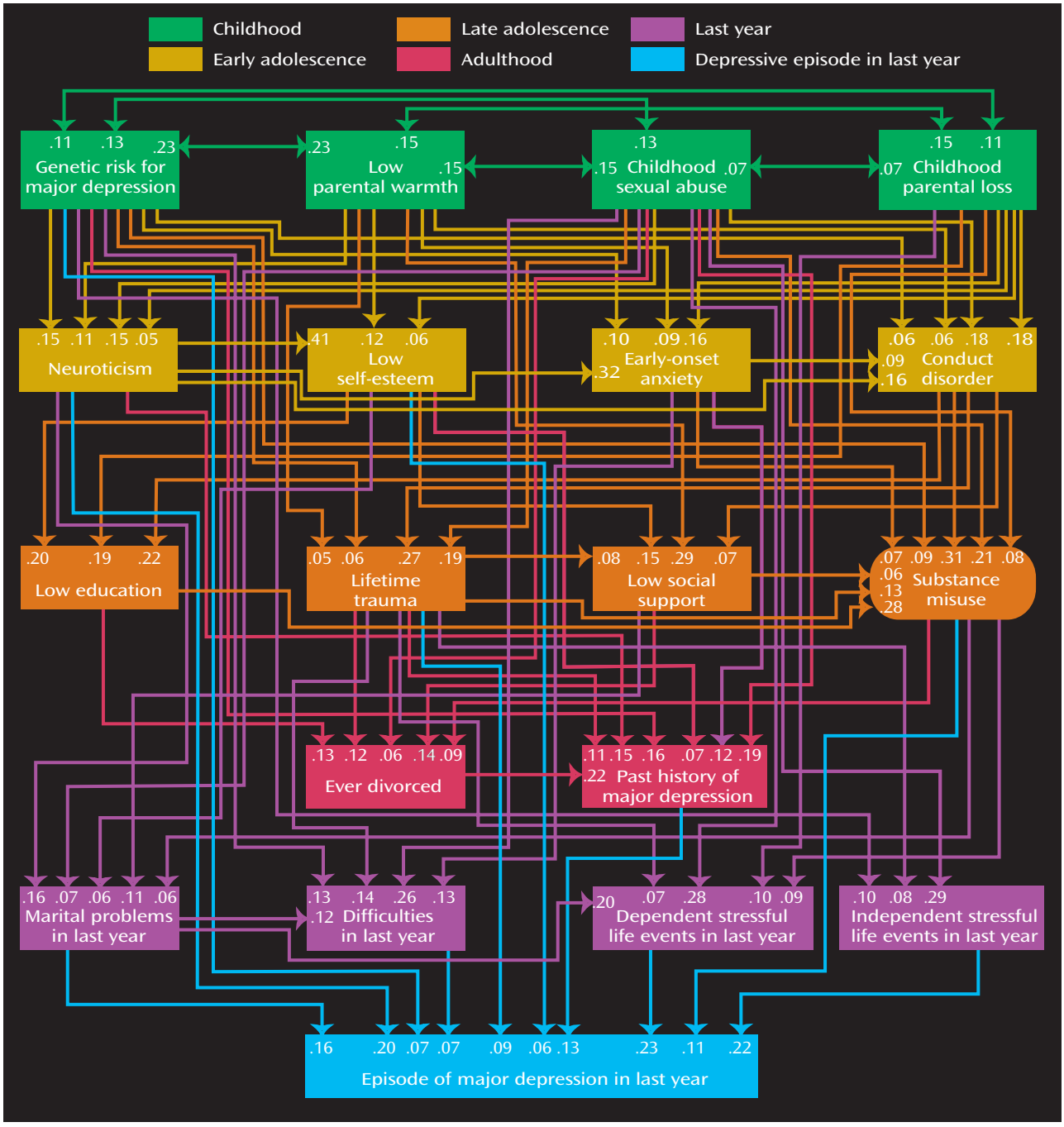
Risk factors of late adolescence. Low educational attainment uniquely predicted only substance misuse and risk for divorce (Figure 1). Lifetime trauma predicted low social support, substance misuse, risk of divorce, difficulties and independent stressful life events in the last year, and both past history of major depression and major depression in the last year.

Low social support was a unique predictor of substance misuse, risk of divorce, and last-year marital problems.

Substance misuse predicted risk for divorce and marital problems, dependent stressful life events, and major depression in the last year.

"Adult" risk factors. Both divorce and past history of major depression were predicted by an array of upstream variables (Figure 1). "Ever divorced" uniquely predicted only past history of major depression, which in turn uniquely predicted only risk for an episode of major depression in the last year.

FIGURE 1. Results of the Best-Fit Model for the Prediction of an Episode of Major Depression in the Last Year Among 2,935 Men in Male-Male Twin Pairs[a]

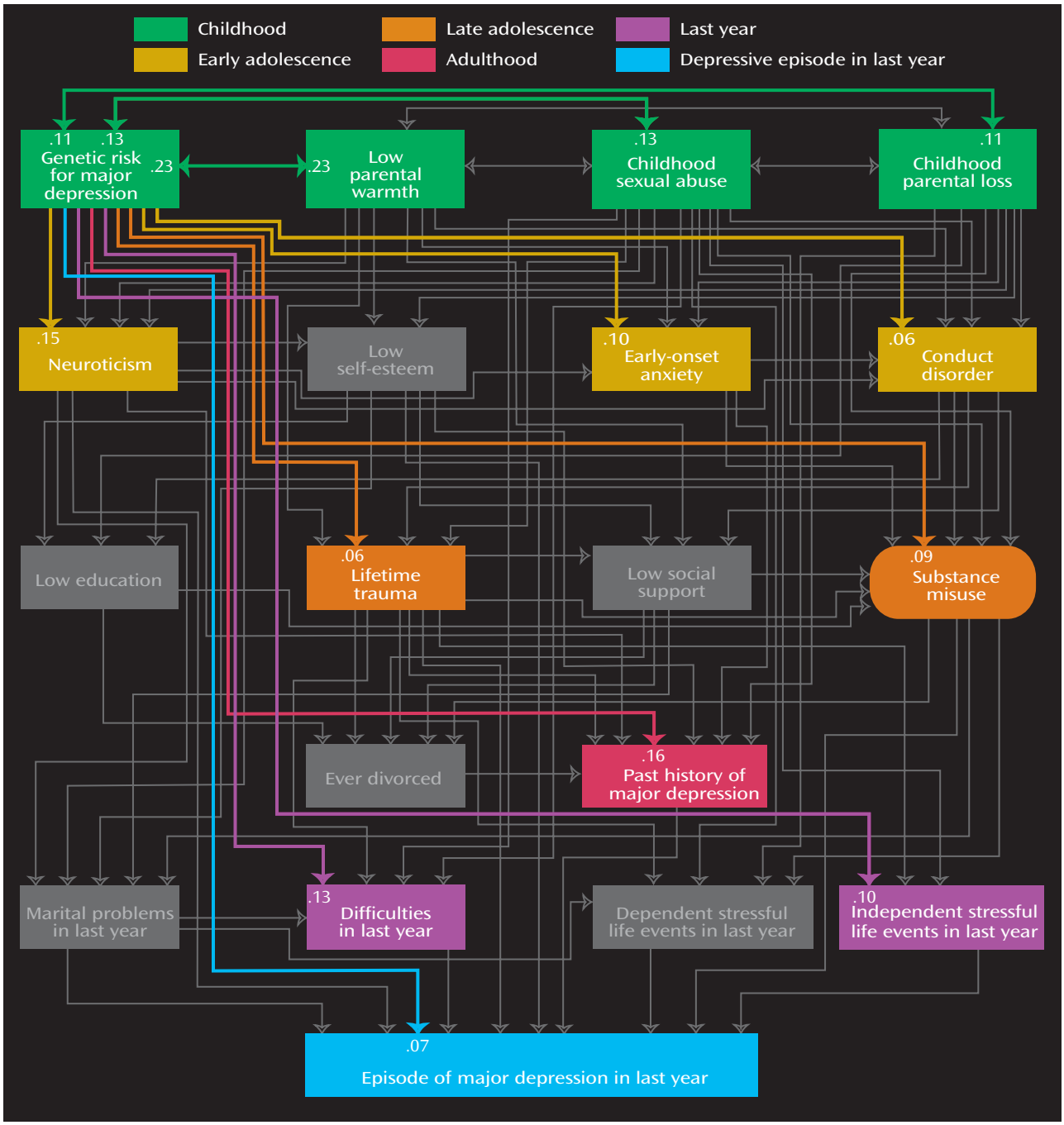


[a] Two-headed arrows represent correlation coefficients. One-headed arrows represent path coefficients or standardized partial regression coefficients. Latent variables—indexed by observed variables in a measurement model—are depicted in ovals while observed variables are depicted in rectangles. All variables have estimated residual variance not depicted in the figure. See text for a description of the variables.

Last-year risk factors. All four measures of environmental adversity in the last year, two reflecting "difficulties" and two stressful life events, were all predicted by a moderate number of upstream variables in the model (Figure 1). All four of them predicted last-year onset of major depression, with the impact of events being stronger than that of difficulties.

Episode of major depression in the last year. As depicted in Figure 3, the direct influences on risk for major depression in men are varied and include genetic risk, neuroticism, low self-esteem, lifetime traumas, substance misuse, past history of major depression, and all four last-year risk factors. In order of magnitude, the five strongest risk factors were last-year dependent and independent

FIGURE 2. Paths and Correlations That Involve the Variable "Genetic Risk for Major Depression" From the Best-Fit Model for the Prediction of an Episode of Major Depression in the Last Year Among 2,935 Men in Male-Male Twin Pairs[a]



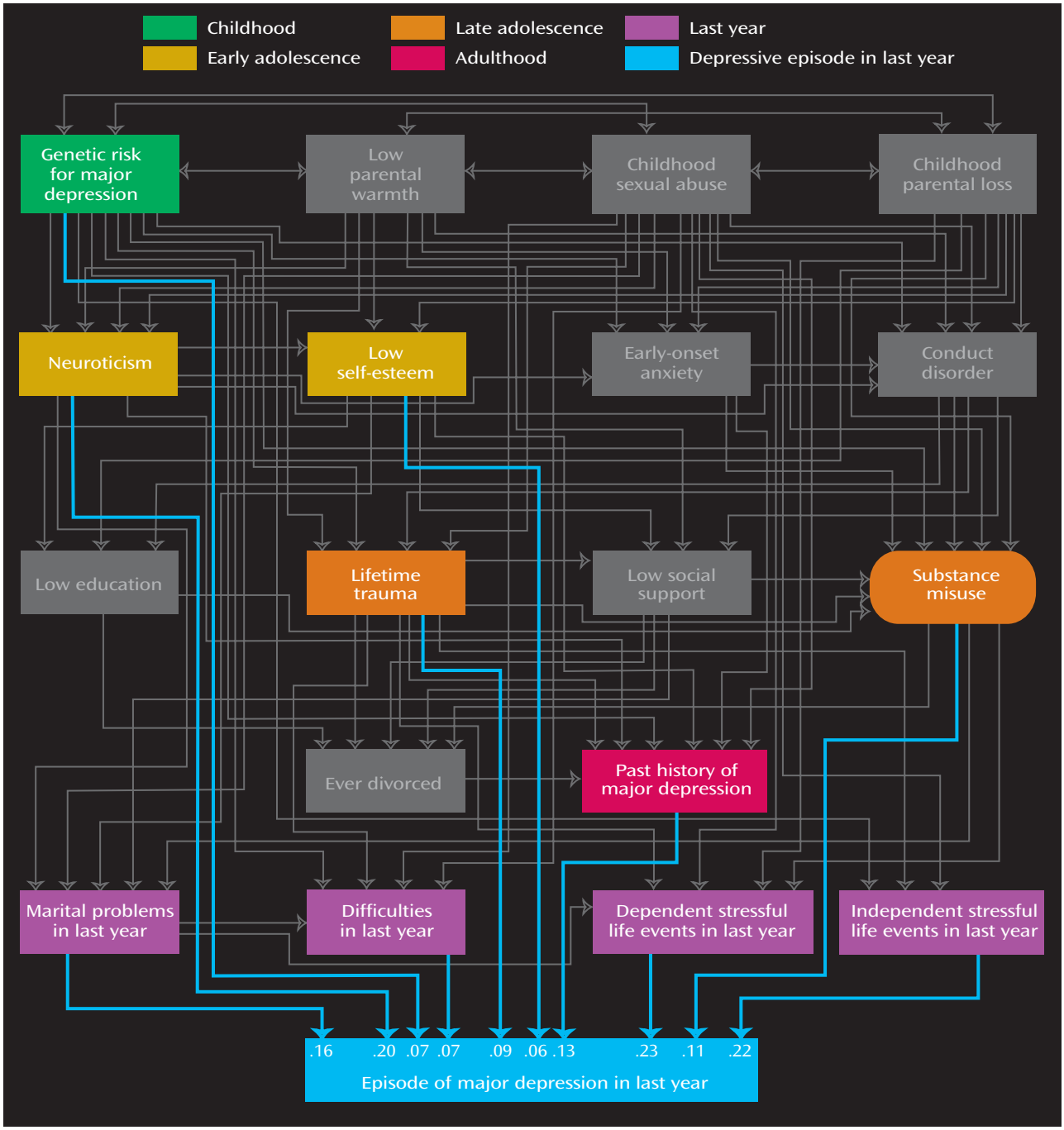
[a] Two-headed arrows represent correlation coefficients. One-headed arrows represent path coefficients or standardized partial regression coefficients. Latent variables—indexed by observed variables in a measurement model—are depicted in ovals while observed variables are depicted in rectangles. All variables have estimated residual variance not depicted in the figure. See text for a description of the variables.

stressful life events, neuroticism, last-year marital problems, and past history of major depression.

Pathways to Depressive Illness

As with women (2), our best-fit model suggested three pathways to major depression in men, characterized by internalizing symptoms (genetic risk factors, neuroticism, low self-esteem, early-onset anxiety, and past history of major depression), externalizing symptoms (genetic risk factors, conduct disorder, and substance misuse), and adversity and interpersonal difficulty (low parental warmth, childhood sexual abuse and parental loss, low education, lifetime trauma, low social support, history of divorce, past history of major depression, marital problems, and stressful life events)

FIGURE 3. Paths That Involve the Variable "Episode of Major Depression in the Last Year" From the Best-Fit Model for the Prediction of an Episode of Major Depression in the Last Year Among 2,935 Men in Male-Male Twin Pairs[a]



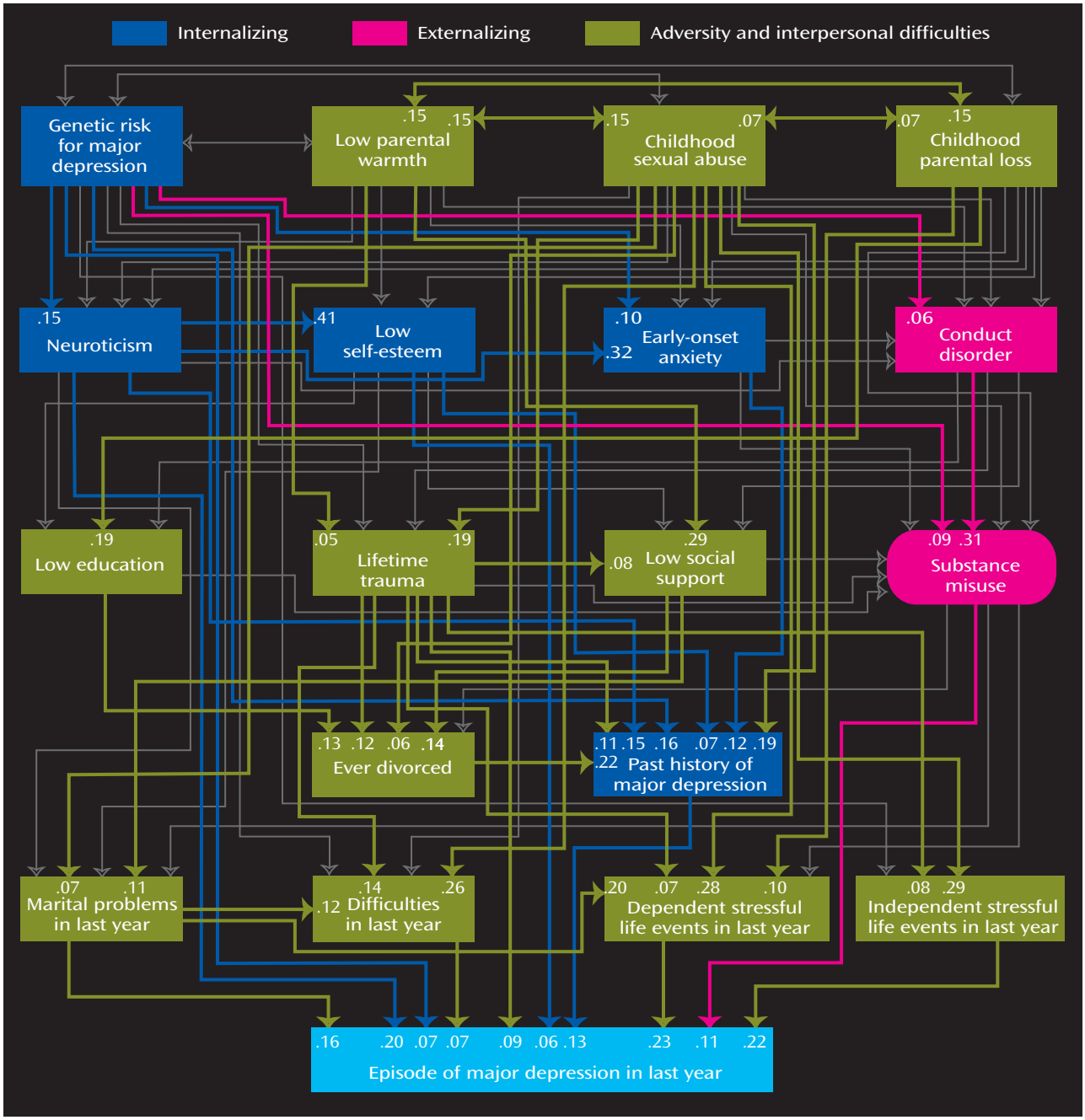
[a] Two-headed arrows represent correlation coefficients. One-headed arrows represent path coefficients or standardized partial regression coefficients. Latent variables—indexed by observed variables in a measurement model—are depicted in ovals while observed variables are depicted in rectangles. All variables have estimated residual variance not depicted in the figure. See text for a description of the variables.

(Figure 4). As in women, a number of cross-influences were seen between these three pathways. Genetic risk factors for major depression contributed to all three pathways. Several other variables in the internalizing and externalizing pathways predicted increased interpersonal difficulties. Early adversity was strongly related to later externalizing symptoms and more weakly to later internalizing symptoms.

Qualitative Differences Between Models in Men and Women

A comparison of the best-fit model in this report and that reported in women (2) suggests six broad conclusions. First, the model in men contained more paths than in the women (76 versus 64), probably partly because of greater statistical power in the larger male sample. Second, the overall similar-

FIGURE 4. Three Broad Pathways to Major Depression in the Best-Fit Model for the Prediction of an Episode of Major Depression in the Last Year Among 2,935 Men in Male-Male Twin Pairs[a]



[a] Only paths that are within the three pathways are highlighted. The internalizing pathway is depicted in dark blue, the externalizing pathway is shown in pink, and the adversity and interpersonal difficulties pathway is depicted in olive green. Genetic risk for major depression is depicted in dark blue as it is a prime variable in the internalizing pathway. However, it also plays a role in the externalizing pathway, as it uniquely contributes to risk for both conduct disorder and substance misuse. Two-headed arrows represent correlation coefficients. One-headed arrows represent path coefficients or standardized partial regression coefficients. Latent variables—indexed by observed variables in a measurement model—are depicted in ovals while observed variables are depicted in rectangles. All variables have estimated residual variance not depicted in the figure. See text for a description of the variables.

ities in the two models far outweigh the differences. The general pattern of risk factors and their relationship through developmental time were broadly congruent in the two sexes.

Third, differences emerged in the spectrum of action of genetic factors for major depression. In both sexes, the final model contained paths from genetic risk factors to neuroticism, substance misuse, lifetime traumas, past history of major depression, and risk of major depression in the last year. Across genders, genetic risk for depression is partly mediated by effects on personality, increased ex-

posure to traumatic events, and substance misuse. Furthermore, in both men and women, when the analysis controlled for the impact of genetic factors on prior episodes, individuals at high genetic risk remained at increased risk for further episodes into middle adult life. In men, but not in women, genetic risk factors for major depression uniquely predicted risk for early-onset anxiety and conduct disorder. While in women genetic risk factors for major depression increased risk for divorce, in men they increased exposure to difficulties and stressful life events in the last year. Perhaps because of greater statistical power in this larger sample, genetic risks for major depression had a broader spectrum of action in men than in women.

Fourth, childhood parental loss had more diverse and potent effects in men than in women. In women, parental loss uniquely contributed only to risk for substance misuse. In men, such loss predicted all four early adolescent risk factors, low educational achievement, substance misuse, and dependent stressful life events.

Fifth, low self-esteem is a more potent variable in men than in women. While in women low self-esteem predicted only low educational attainment, in men it increased risk for a total of five downstream variables, including lifetime and last-year major depression.

Sixth, two plausible hypotheses with which we began this study were not supported. We expected childhood sexual abuse to have more potent effects in women than men. This was not seen. We also predicted that the pathway to major depression running through conduct disorder and substance misuse would be more prominent in men than in women. This was also not strongly supported. In men the best-fit model contained a direct path from substance misuse to last-year major depression, and such a path was not present in women. However, in women the model contained a direct path from conduct disorder to last-year major depression and a direct path from substance misuse to past history of major depression, both of which were lacking in the men.

Discussion

We sought to derive empirically an integrated, developmental model for the etiology of major depression in men using methods as comparable as possible to those in our previous study of women (2). Given the complexity of our model and the sample size to which it was applied, its fit was excellent, demonstrating a good balance of parsimony and explanatory power.

Although our current model was slightly less successful at predicting risk for major depression in men (48.7% of the variance) than our prior model in women (52.1%) (2), the general outlines of the results were similar in the two sexes. The present findings, in an independent sample, obtained with comparable measures and methods, broadly replicate our previous results in women.

Methodological Limitations

Since we previously outlined methodological limitations of our modeling (2), we review them here briefly. First, these models assume a causal relationship between predictor and dependent variables. The validity of this assumption varies across our model. Some of the intervariable relationships that we assumed take the form of $A \rightarrow B$ may be truly either $A \leftarrow B$ or, more likely, $A \leftrightarrow B$.

Second, a number of variables were assessed by long-term memory and may be subject to recall bias. Within the limits of a two-wave design with a cohort in early to middle adulthood, we tried to minimize this problem by using multiple reporters (e.g., for parental warmth), recording objective events less susceptible to recall bias (e.g., parental loss, divorce, educational level), assessing variables prospectively (i.e., at our first interview) when possible, and measuring a number of key constructs over the last year (including stressful life events and depressive onsets), thereby reducing the time frame of recall.

Third, the sequence of variables in our model was only approximate. We evaluated the validity of our ordering by fitting 10 additional models in which we took more "upstream" variables and moved them "downstream." In nine of these, the model fit deteriorated, often dramatically. In one model, the fit improved modestly but contained implausible causal assumptions (i.e., that low self-esteem, neuroticism, and low social support cause parental loss). In aggregate, these analyses support the appropriateness of the sequence of variables in our model.

Fourth, our model assumes that multiple independent variables act additively and linearly in their impact on risk for major depression. This is unlikely to be true. In this sample, for example, high levels of neuroticism increased sensitivity to the depressogenic effects of stressful life events (20).

Fifth, this sample consisted of adult white male twins born in Virginia. With respect to the rates of psychopathology—including depressive symptoms and major depression—twins are probably representative of the general population (21, 22). Furthermore, our 1-year prevalence of major depression (6.1%) was midway between that reported in the original National Comorbidity Survey (7.7%) (23) and that found in the recently completed National Comorbidity Survey replication (4.7%) (personal written communication, R. Kessler, October 2005), suggesting that our sample is likely to be broadly representative of American men. However, our results might differ in men from other ethnic groups.

Sixth, our model probably underestimates the impact of genetic factors on the etiology of major depression as our measure of genetic risk was indirect and we did not in-

clude the well-known genetic influences on other key variables, such as neuroticism, anxiety disorders, conduct disorder, and substance use.

Seventh, differences between the present model and that presented previously in women (2) could arise from four sources that cannot be easily distinguished: 1) true differences, 2) variation in measures, 3) greater power in the male sample, and 4) statistical fluctuations. Our measure of "low parental warmth" is probably less potent than our parallel variable in our female sample (disturbed family environment) because it is a poorer measure of early family problems. Modest differences between the two models should not be overinterpreted. For example, a direct path from substance misuse to last-year major depression is seen in men but not women (2). However, this may not be a major difference because in both sexes, conduct disorder and substance misuse were strongly related. In women, conduct disorder but not substance misuse predicted depressive onsets. In men, the opposite effect was seen.

Conclusions

Major depression in men is a complex, multifactorial disorder, the liability to which is influenced by a broad array of risk factors that act at different stages of development. Variables that influence risk for major depression in men include genetic and temperamental factors, psychosocial adversity both early in life and in adulthood, childhood anxiety and conduct disorders, and substance misuse. A comparison of these results with those obtained previously in women, by using parallel methods and measures (2), suggests only modest differences. While a few variables appeared to differ meaningfully across the two, the overall pattern of results was similar. These results suggest that, from an etiologic perspective, major depression is largely the same disorder in men and women.

As in women, these results further illustrate the complexity of the "gene to phenotype" pathway. Individuals at elevated genetic risk for major depression are likely to be exposed to higher rates of childhood adversity, to have higher levels of neuroticism, to have higher rates of early-onset anxiety disorder and substance misuse, and to select themselves into more difficulties and stressful life events in adulthood, all of which in turn increase risk for a depressive outcome. Genes almost certainly influence risk for major depression by traditional "inside the skin" physiological pathways (i.e., by altering susceptibility to dysphoria as instantiated in selected brain systems). However, "outside the skin" pathways, whereby susceptibility genes alter exposure to drug abuse and psychosocial adversities, are also likely to prove critical. In multifactorial disorders such as major depression, gaining a deeper understanding of etiology will be substantially aided by examining the joint effects of multiple risk factor domains.

Received Jan. 3, 2005; revision received March 8, 2005; accepted April 25, 2005. From the Virginia Institute for Psychiatry and Behavioral Genetics and the Departments of Psychiatry and Human Genetics, Medical College of Virginia of Virginia Commonwealth University. Address correspondence and reprint requests to Dr. Kendler, Department of Psychiatry, Medical College of Virginia, P.O. Box 980126, Richmond, VA 23298-0126; kendler@hsc.vcu.edu (e-mail).

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