A Population Based Twin Study of Sex Differences in Depressive Symptoms

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Depressive symptoms reflect depressed mood over a relatively short period of time and are measured using symptom checklists such as the SCL-90. There is some evidence that depressive symptoms are associated with major depression (MD), which is a clinically diagnosed psychiatric illness. Genetic studies of depressive symptomatology suggest a role for genetic factors as well as unique environmental influences. While epidemiological research suggests that depressive symptoms may be influenced by sex-specific factors, few genetically informative findings support this result entirely. We used data from male and female same-sex and opposite-sex twin pairs to assess the extent to which genetic, shared and unique environmental factors influence depressive symptoms. Furthermore, we tested for the presence of qualitative and quantitative sex differences in depressive symptoms. Our results suggest that similar to other studies, depressive symptomatology is moderately heritable (31%) with no evidence for shared environmental factors. Our best fitting model suggests that there are no qualitative or quantitative sex differences in depressive symptoms. Our analyses suggest that while there may be mean differences in the levels of depressive symptoms across sexes, the genetic and environmental factors that predispose males and females to depressive symptoms are not different.

Depressive symptomatology may be defined as a short period in time when an individual experiences depressed mood. Items assessing depressive symptoms are fairly similar to those used to assess the more pathological form of clinically diagnosed major depression (MD). For example, individuals with depressive symptoms will often report feeling "blue" for no reason, feelings of worthlessness and moderate levels of inappropriate guilt. They may also experience loss of sexual interest and hopelessness coupled with overwhelming fatigue in accomplishing daily tasks.

In contrast to clinically assessed MD, depressive symptoms are often assessed by responses to self-report questionnaires and generally reflect symptomatology over a relatively short period of time. Nevertheless, depressive symptoms show some stability over time with one study estimating that between 40 and 76% of the variance in self-report scores is due to stable symptomatology (Duncan-Jones et al., 1990).

Epidemiological research suggests that depressive symptoms are influenced by a variety of risk factors. These include socioeconomic status, alcohol and drug use, coping styles, social roles and stressful life events (Bebbington, 1996; Bovasso, 2001; Jardine et al., 1984; Kendler et al., 2001b; Kendler et al., 2002a; Kendler et al., 1997). Depressive symptoms may also be associated with MD. One study of the relationship between MD and depressive symptoms using data from a sample of 703 female twin pairs showed a correlation of +0.70 for the additive genetic influences between liability to MD and liability to depressive symptoms (Foley et al., 2001). Thus, approximately two-thirds of the variance for liability to MD is shared by the stable component of depressive symptoms, indicating a substantial relationship between MD and depressive symptoms.

Some studies have examined the etiologic role of genetic factors influencing depressive symptoms (Gatz et al., 1992; Mackinnon et al., 1990; Silberg et al., 1990; Jardine et al., 1984; Clifford et al., 1984; Kendler et al., 2002a; Kendler et al., 2003a; Sanathara et al., 2003; Kendler et al., 2003b; Kendler et al., 2002b; Khan et al., 2002; Fanous et al., 2002; Sullivan et al., 2002; Kendler et al., 2001a; Kendler & Gardner, 2001; Kendler et al., 2001b). Findings suggest that genetic factors play a significant role in the presentation of depressive symptoms (Gatz et al., 1992; Kendler et al., 1994) and that shared environment is not a significant factor. Heritability estimates of depressive symptoms range from 0.22–0.37%. However, few studies have analyzed sex differences in

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the genetic and environmental influences on depressive symptoms.

There is evidence that non-shared environmental factors predict depressive symptoms, and the magnitude of these factors may vary for men and women (Gatz et al., 1992). This suggests that individual-specific environmental factors may play a pivotal role in the etiology of depressive symptoms and further, that the importance of these factors may vary across sexes. Several environmental factors have been shown to have an effect on the expression of depressive symptoms including constraining social factors, coping styles, role-playing at home, employment status and work related stress-coping factors in men and women. Hormonal cycles in women also seem to predispose women to phases of depression (Bebbington, 1996). These sex differences in risk factors may contribute to the mean level gender differences seen in the etiology of depressive symptoms.

In this study, we use a combined sample of MZ and DZ male, female and opposite sex twin pairs to determine quantitatively (1) whether genetic and environmental factors exert a similar magnitude of influence in men and women for risk to depressive symptomatology and qualitatively (2) whether the genetic and environmental risk factors predisposing the individual to depressive symptomatology are the same in men as in women.

Subjects and Methods

Sample

The twin pairs in this study are drawn from the population-based Virginia Twin Registry, formed from a systematic review of all birth certificates in the Commonwealth of Virginia. The data were obtained from the first wave of interviews conducted individually for female-female twin pairs and male-male/male-female twin pairs. Details are presented elsewhere (Kendler & Prescott, 1999).

The sample for these analyses consists of 5092 males and 3691 females. The sample included 3735 complete twin pairs, 16 complete sets of triplets, one complete set of quadruplets and 1257 individual twins with a non-participating co-twin. The number of individuals and complete twin pairs in each zygosity (MZ and DZ) group are presented in Table 1. The zygosity of twins was determined by responses to questions relating to their physical similarities and how often people confused the twins when they were children. Questionable cases were resolved using photographs and DNA testing (Spence et al., 1988). The mean age for the sample is 33.40(*SD* = 9.16) and the mean years of education is 13.35 (*SD* = 2.30).

Depressive Symptom Checklist

Responses to a self-report symptom inventory were obtained from each participant in the study using a 30-item subset of the SCL-90 (90-item Symptom Check List; Derogatis et al., 1970). The items in the questionnaire fall under four SCL-90 subscales: depression (10 items), somatization (5 items), anxiety (7 items) and phobic anxiety (5 items). Three items that deal with sleep difficulty were also included. The participants were instructed to consider the list of problems and indicate to what extent that problem had bothered them "over the past 30 days including today". Responses were graded on a scale of 5 ranging from (1) *not at all* to (5) *extremely*.

For this study, the following 10 items from the depression subscale were employed: #5 loss of sexual interest or pleasure; #14 feeling low in energy; #22 feeling of being "trapped" or "caught"; #26 blaming yourself for things; #30 feeling blue; #31 worrying too much about things; #32 feeling no interest in things; #54 feeling hopeless about the future; #71 feeling everything is an effort and #79 feelings of worthlessness.

Item selection was based on regression analyses that indicated that these items accounted for 95% variance in the summary score derived from the total set of 13 SCL depression items (Foley et al., 2001). The scores were summed across the items to form a single scale score ranging between a minimum of 10 to a possible maximum of 50 (Cronbach alpha of 0.88). The summed score was then transformed into an ordinal variable using an approximate decile split to account for the skewness in distribution. Thus, categories ranged from 0–9. Thresholds corresponding to the percentage of individuals within each category were estimated in the structural equation modeling analyses.

Twin Modeling

Data were analyzed using the structural equation modeling program Mx (Neale, 1990). Models were fit to covariance matrices created from the raw data. Estimates of genetic and environmental influence were obtained using maximum likelihood estimation.

In standard ACE modeling, the variations in a phenotype are distributed into additive genetic (A), shared environmental (C) and individual-specific environmental (E) variance (Neale & Cardon, 1992). Models were fitted to test for qualitative and quantitative sex differences. Qualitative sex differences were assessed by allowing the genetic or the shared environmental correlation across sexes to vary from 1.0 and testing whether this resulted in a significant improvement in model fit. The quantitative sex differences were assessed by allowing the magnitude of genetic and environmental parameters to vary across the sexes. This model was compared for fit with the model where the genetic and environmental parameters were constrained to be the same in both sexes. All models were compared to a saturated model for goodness-of-fit (Williams, 1994). The best fit model was selected by the Akaike's Information Criterion (AIC) which is an index of both goodness-of-fit and parsimony (Akaike, 1987).

Results

Table 1 presents the descriptive statistics and the relevant polychoric correlations for each zygosity group.

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The correlations in the MZ twin pairs were substantially higher than the correlations in the DZ twin pairs in both sexes, suggesting a significant contribution of genetic factors in depressive symptoms. Furthermore, The polychoric correlation for the liability to depressive symptoms in DZ opposite sex twin pairs (r = 0.14) was similar to the DZ correlations in the same sex pairs. This suggests that there may not be qualitative differences between sexes for depressive symptoms.

Before conducting the genetic analyses, we examined if the thresholds varied by gender, zygosity, or by gender of co-twin. In the same sex pairs, thresholds did not vary across zygosity (χ^2 = 10.74, df = 18, p = .91) or across members of the twin pair (χ^2 = 35.81, df = 36, p = .48). There was also no evidence for variation in thresholds by gender of the co-twin, indicating that twins from opposite-sex pairs were similar to twins from same-sex pairs (χ^2 = 16.51, df = 18, p = .56). However, the thresholds for gender were significantly different (χ^2 = 185.85, df = 9, p < .0001). This indicates that the distribution of depressive symptoms differs for males and females. Consequently, the thresholds in men and women were allowed to vary across sexes for further analyses.

Table 2 presents the results obtained from the structural equation modeling. Model 1, in which additive genetic (A), shared environmental (C) and unique environmental (E) influences were allowed to vary across sexes, was fitted first. This model fitted the data well. Next, we tested for qualitative sex differences. In Model 2, r_g (the genetic correlation across sexes) was allowed to vary from 1.0. This model estimated a correlation of 0.90 for genetic influences across sexes and this was not significantly different from the theoretical correlation of 1.0. We performed a similar analysis where the correlation for shared environmental influence (r_c) was allowed to vary across sexes (Model 3). Model 3 did not significantly improve the fit over the model in which r_c was constrained to 1.0 (r_c = 0.79 in Model 3). Thus, there was no evidence for qualitative gender differences in depressive symptoms. In other words, we could reject the hypothesis that the genes and common environmental influences that predisposed males and females to depressive symptoms overlapped completely across sexes.

Next, quantitative sex differences were analyzed. In Model 4, we constrained A, C and E to be equal across sexes (but not to each other). This model fit the data as well as the ACE unequal model where A, C and E were independently estimated in males and females. This indicated that there were no sex differences in the magnitude of genetic or environmental influences across sexes. Working from Model 4, we compared the equal ACE model (Model 4) to the AE model (Model 5) which assumes that variation in depressive symptoms is entirely due to genetic predisposition and individual specific environmental

Table 1

Descriptive Statistics for Twin Pairs in Five Zygosity Groups with Number of Twins and Twin Pairs, Mean Score for Depressive Symptoms and Polychoric Correlation

Group	Ntwins	Npairs	Mean Score (*SD*)	Polychoric correlation
Same Sex twin pairs				
MZ males	1950	855	4.09 (5.00)	0.30
MZ females	1141	498	5.59 (5.67)	0.33
DZ males	1568	643	4.34 (5.31)	0.18
DZ females	839	365	6.02 (6.32)	0.13
Opposite sex twin pairs				
DZ males	1574	1403	4.63 (5.80)	0.14
DZ females	1711		5.56 (5.80)	

Table 2

Parameter Estimates for Model-fitting Procedure

				Males			Females				
No.	Model	*df*	AIC	a^2	c^2	e^2	a^2	c^2	e^2	r_g	r_c
1	ACE unequal	8761	–81.8	0.31	0.00	0.68	0.31	0.00	0.69	a	a
2	Free r_g	8760	–80.5	0.28	0.04	0.68	0.32	0.03	0.65	0.90	a
3	Free r_c	8760	–80.4	0.25	0.06	0.68	0.31	0.08	0.61	a	0.79
4	ACE equal	8764	–84.9	0.30	0.01	0.69	0.30	0.01	0.69	a	a
5	AE equal*	8765	–87.4	0.31	—	0.69	0.31	—	0.69	a	—
6	CE equal	8765	–60.2	—	0.20	0.80	—	0.20	0.80	—	a
7	E equal	8766	+76.8	—	—	1.00	—	—	1.00	—	—

Note: *Best-fitting model.
AIC is based on comparison to a saturated model.
a = parameter is fixed to 1.0 in the model.

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factors. Model 5 fit the data as well as the equal ACE model. The AE model was preferred to the ACE model by the AIC criterion because of greater parsimony. The CE model (Model 6), which assumes that resemblance between twins for depressive symptoms is entirely due to shared environmental and unique environmental influences and not due to genetic factors, caused a significant deterioration of fit. Finally, the E model (Model 7), which assumes no resemblance in twins for depressive symptoms, fitted very poorly and was rejected. Based on the best-fitting sex-equal AE model, the heritability of liability to depressive symptoms was estimated at 31% (95% confidence interval [CI], 27%–36%). The remaining 69% (95% confidence interval [CI], 64%–73%) variance in liability to depressive symptoms was due to individual-specific environmental influences.

Discussion

Some studies propose different etiologies for depressive symptoms in males and females. We sought to estimate the magnitude of the genetic, shared environmental and unique environmental influences that contribute to depressive symptoms and to test whether these factors exerted a similar magnitude of influence for both males and females. In addition, we analyzed whether the genetic and shared environmental influences predisposing males and females to depressive symptoms were the same for both sexes.

In our data, the correlation in depressive symptoms between the DZ same sex and DZ opposite-sex did not differ significantly from each other. Formal model-fitting revealed that the genetic factors that influence the risk for depressive symptoms are the same in males and females. Our study also found that the heritability of the liability to depressive symptoms was moderate and was the same across sexes, with an estimate of 0.31. Thus, although we found significant differences in mean levels of depressive symptoms, we found no evidence for qualitative or quantitative gender differences in the etiology of depressive symptoms. In addition, the variance due to common environmental influences on depressive symptoms was not significantly greater than zero.

We are aware of four other studies that analyzed sources of individual differences in depressive symptoms. In a study involving two data sets (19,203 individuals recruited through the AARP (American Association of Retired Persons and their relatives and 11,242 individuals from the MATR), the tetrachoric correlations obtained were similar to those found in our sample. The heritability of liability to depressive symptoms for the MATR sample was 29.7% and for the AARP sample was 36.7%. This study also found equal estimates of heritability in males and females (Kendler et al., 1994). Our results are also in agreement with another study of identical and fraternal twin pairs, some reared apart (n = 229) and some together (n = 252) that used the CES-D scale (Gatz et al., 1992). The study reported that separate models for males and females for depressive symptoms could not be supported. In other studies, while no qualitative differences were detected, heritability of depressive symptoms was reported to be moderately higher in females than in males (Jardine et al., 1984; Mackinnon et al., 1990). However, these studies utilized very large samples and included multiple family relationships (spousal, parent-offspring, sibling) that may account for the detection of the increase in heritability estimates in females.

Epidemiological studies have proposed that there is a greater prevalence of depressive symptoms in females. One report also suggests that while females report depressive symptoms more frequently, males suffer to a greater extent (Kluger, 2003). We did note mean differences in the levels of depressive symptoms across sexes. Several factors such as hormonal activity, social roles and coping styles, could be responsible for these differences (Bebbington, 1996). However, this did not translate into differences in the magnitude or the nature of the genetic or environmental factors influencing depressive symptoms. This suggests that despite differences in prevalence, the etiologic factors for depressive symptoms are the same in males and females. This may be partially influenced by the mean age of the sample (mid-30s). Bebbington et al. (2003) noted that sex differences were less apparent in middle-aged cohorts.

These results are an interesting contrast to the results obtained for the related phenotype of major depression (MD). Gender differences in genetic influence on MD have been previously analyzed using the same sample. Both qualitative (Kendler & Prescott, 1999; Kendler et al., 2001a) and quantitative (Kendler et al., 2001a) gender differences were found for MD. Although we used the same sample for our analysis, we found neither qualitative nor quantitative differences for depressive symptoms. This is interesting considering that at least among the females in this sample, the genetic correlation between liability to MD and liability to depressive symptoms is high (+0.70) (Foley et al., 2001). This suggests that there may be greater gender differences that influence the episodic nature of MD than the "personality-like" features of depressive symptoms.

Limitations

The results of this study should be interpreted considering three potential limitations in methodology.

First, the data used for analysis is only from one wave of interviews. We cannot be sure how much of the E measured has been influenced by measurement errors. Relatedly, we were unable to measure sex differences in the individual-specific environmental influences. Our models did not include measured environment variables and this may have decreased our power to detect sex differences in environmental influences. Second, our sample consisted only of Caucasians and we cannot be certain of similar results

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for other ethnic groups. Third, our study used responses to the SCL-90, which is a popular scale for assessment of self-reported symptoms of depression (Gatz et al., 1992; Gibbons et al., 1993; Radloff, 1977). Measurements on other scales were not conducted but studies conducted on other scales like the CES-D scale have shown similar results.

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