The Genetic Epidemiology of Phobias in Women
The Interrelationship of Agoraphobia, Social Phobia, Situational Phobia, and Simple Phobia

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- In 2163 personally interviewed female twins from a population-based registry, the pattern of age at onset and comorbidity of the simple phobias (animal and situational) — early onset and low rates of comorbidity — differed significantly from that of agoraphobia — later onset and high rates of comorbidity. Consistent with an inherited “phobia proneness” but not a “social learning” model of phobias, the familial aggregation of any phobia, agoraphobia, social phobia, and animal phobia appeared to result from genetic and not from familial-environmental factors, with estimates of heritability of liability ranging from 30% to 40%. The best-fitting multivariate genetic model indicated the existence of genetic and individual-specific environmental etiologic factors common to all four phobia subtypes and others specific for each of the individual subtypes. This model suggested that (1) environmental experiences that predisposed to all phobias were most important for agoraphobia and social phobia and relatively unimportant for the simple phobias, (2) environmental experiences that uniquely predisposed to only one phobia subtype had a major impact on simple phobia, and had a modest impact on social phobia, and were important for agoraphobia, and (3) genetic factors that predisposed to all phobias were most important for animal phobia and least important for agoraphobia. Simple phobias appear to arise from the joint effect of a modest genetic vulnerability and phobia-specific traumatic events in childhood, while agoraphobia and, to a somewhat lesser extent, social phobia result from the combined effect of a slightly stronger genetic influence and nonspecific environmental experiences.

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Phobias, among the most common of the well-recognized psychiatric syndromes, are of particular interest to genetic epidemiologists because several competing etiologic theories have been developed, each of which suggests that phobias arise mainly from one of the three domains of risk factors: individual-specific environment, family environment, and genes. One school of thought has suggested that phobias arise as a result of classic conditioning from the accidental pairing of benign and fear-inducing stimuli. This theory, which postulates that phobias should be entirely environmental in origin, would predict that the familial aggregation of phobias, which would result only from the correlated exposure among family members to such a coincidental pairing of stimuli, is likely to be modest.

Social learning theory provides a basis of another behavioral theory of phobias. In humans and nonhuman primates, the fear of objects or situations can be learned from observing the fear responses of others. Since most phobias begin in childhood, other family members, particularly parents, are likely sources for the “vicarious” acquisition of phobias. The social learning theory, therefore, predicts substantial familial aggregation of phobias from shared environmental experiences.

As first observed by Darwin, the choice of feared objects and situations in phobias is not random. This has been explained by two related theories of “inherited phobia proneness”: (1) a “preparedness” to develop conditioned fears of certain stimuli or (2) innate fears that require no learning. Both theories suggest that, through natural selection, humans have evolved an inherited predisposition to form phobic reactions to certain stimuli, but they differ as to whether conditioning is required to manifest this predisposition. It is probable that phobia proneness would evolve through stabilizing selection in which a moderate level produced optimal fitness and fitness declined when an individual became either too phobia prone or insufficiently phobia prone. Since such selection usually results in substantial additive genetic variation in populations, the inherited phobia proneness theory predicts significant genetic influences on the predisposition to phobias.

THE GENETICS OF PHOBIAS

Information is available to evaluate these three models preliminarily. Several studies, using a twin or twin-family design, have found that genetic factors and individual-
specific environment, but not family environment, play an important role in the origin of self-reported phobialike fears. We are aware of six studies of the familial aggregation of clinically defined phobias. Four family history studies, three beginning with agoraphobic probands and one with social phobic probands, have found evidence of the familial aggregation of phobias. Using a family study design, Noyes et al found, in relatives of agoraphobic vs control probands, significantly increased rates of agoraphobia but not of social or simple phobia. Beginning with probands with simple phobia, Fyer et al, using direct interviews, found significantly higher rates for simple but not social phobia in relatives of affected vs control probands.

Two twin but no adoption studies have examined clinically defined phobias. Carey and Gottesman, examining 21 twin probands hospitalized with phobia, found low and similar concordance rates in monozygotic (MZ) and dizygotic (DZ) twins for treated phobia. However, using the broad definition of phobic "symptoms or features," they found a much higher concordance rate in MZ (88%) than in DZ (38%) twins. Torgersen studied 12 twin probands in Norway with a primary diagnosis of phobia and found that none of the cotwins were phobic. However, two of the four MZ cotwins had another anxiety disorder compared with none of the eight DZ cotwins.

Although clinically defined phobias appear to be familial, we do not know whether this results from genetic factors and/or shared environmental factors. The two twin studies of phobias had quite small samples, ascertainment only treated cases (which constitute a small and unrepresentative proportion of affected individuals), and assessed twins with knowledge of the clinical status of the cotwin.

**SUBTYPES OF PHOBIA: THE SAME OR DIFFERENT?**

The phobias are a set of syndromes all of which share an irrational and fearful avoidance of objects or situations that cannot be explained as a function of the threat truly posed thereby. However, the phobias also differ in important ways. In simple phobias, the phobic stimulus is well circumscribed, while in social phobia and particularly agoraphobia, the phobic stimuli are relatively diffuse. Furthermore, Klein argued that the development of agoraphobia, as a sequel of spontaneous panic attacks, is qualitatively different from that of other phobias.

What is the relationship between the genetic and environmental risk factors for the different subtypes of phobias? Age at onset and patterns of comorbidity suggest meaningful differences between phobic subtypes. Family studies of phobia performed to date have found some evidence of the specificity of familial factors for individual phobic subtypes.

**GOALS**

By examining the presence of any phobia and of four subtypes of phobia as assessed at personal interview in 2163 adult female twins from a population-based twin register, we sought to clarify the role of genetic and environmental factors both in the etiology of phobias and in the interrelationship between the individual phobic subtypes.

**SUBJECTS AND METHODS**

**Sample and Assessment Procedures**

As outlined in detail elsewhere, female-female twin pairs from the population-based Virginia Twin Registry were personally interviewed by social workers who were blind to the clinical status of the cotwin. Zygosity was determined blindly by standard questions, photographs, and, when necessary, DNA testing. Of the eligible twins, 92% were successfully interviewed, 89% in person and 11% by telephone.

Lifetime prevalence was assessed for the following psychiatric disorders by means of an adapted version of the Structured Clinical Interview for DSM-III-R Diagnosis: major depression, generalized anxiety disorder, panic disorder, alcoholism, and eating disorders (anorexia nervosa and bulimia nervosa). A lifetime history of phobias was assessed by an adaptation of the Phobic Disorders section of the Diagnostic Interview Schedule Version III-C, which in turn was based on the DSM-III criteria.

Three significant modifications were made. First, instead of the respondent being asked individually about a series of fears, the fears were grouped into four categories (Table 1), each of which was inquired about in a single question. Second, several modifications were made to the list of 17 specific fears: (1) fear of using public bathrooms was substituted for fear of writing in public; (2) fears of water, thunder, lightning, being alone, buses, and blood or injections were dropped; (3) animal phobias were expanded to include individual fears of bugs, spiders, mice, snakes, and bats, and (4) situational phobias were expanded to separate fear of tunnels, bridges, airplanes, and other high places. While DSM-III mentions fear of bridges and tunnels as typical of agoraphobia, in our interview these fears were considered part of situational phobia. We also inquired about other phobias, and if a phobia described there belonged with one of the four specific subtypes, it was so treated. Other phobias mentioned in response to this question (e.g., fear of water, the dark, driving, and blood) were included in our analysis of "any" phobia but were not counted as belonging to one of the specific subtypes.

Third, instead of interference being asked about with each
specific fear, it was asked about after each of the four specific and one miscellaneous category of unreasonable fears. In the Diagnostic Interview Schedule, which was developed for nonclinical interviewers, the respondent makes the judgment about interference from an irrational fear; in contrast, in our interview, designed for clinicians, the interviewer made this assessment. Our interviewers were trained to rate whether the unreasonable fear had significant objective behavioral impact on the respondent’s life. Of the “unreasonable” fears expressed in our sample, 40.1% were judged to be accompanied by significant interference.

Phobia was defined in this report, then, as the presence of a fear that the respondent recognized as unreasonable and that, in the judgment of the interviewer, significantly interfered with the respondent’s life. For all analyses reported in this article, a twin was considered affected for all subtypes of phobias for which she met criteria.

Fifty-nine interviews were jointly conducted by two interviewers. Reliability was assessed by examining the five groups of unreasonable fears in each of these interviews. The two interviewers agreed on the presence or absence of an unreasonable fear 261 of 265 times (ie, 53 respondents times five subtypes) (agreement rate, 98.5%; k = +.95 ± .02). In the 83 cases in which both raters agreed that an unreasonable fear was present, their rating of interference agreed in 75 cases (agreement rate, 90.3%; k = +.81 ± .07).

Statistical Analysis

Our approach to the analysis of twin data, has been outlined in detail elsewhere,32,39,40 and consists of inferring the action of genetic and environmental risk factors from the way in which affected and unaffected twins are distributed in twin pairs. In this article, we expand on the previously described univariate analyses to conduct a multivariate genetic analysis of the subtypes of phobias. While the goal of univariate genetic analysis is the decomposition of the variance of a trait into genetic and environmental components, in multivariate genetic analysis, the focus shifts to decomposing sources of covariance between traits. To illustrate the difference between univariate and multivariate twin analysis, the concept of latent or unobserved factors is introduced. In a traditional or “phenotypic” factor analysis, latent factors are postulated to cause the resemblance or, more technically, covariation among items. The goal of factor analysis is to explain the correlations between a large number of variables as resulting from the effects of a small number of latent factors. Multivariate genetic analysis is also a method of explaining correlations between multiple items. However, it goes beyond traditional factor analysis in that it provides insight into the causes of resemblance among variables.

In univariate analysis, information regarding the causes of variation is obtained by comparing the resemblance ofMZ and DZ twin pairs for a single variable. In the multivariate case, the correlation between two or more variables is the primary unit of analysis. By comparing the cross-twin, cross-variable correlation in MZ and DZ twins, and contrasting that to the cross-twin within-variable and within-twin cross-variable correlations, the covariation of two or more variables can be partitioned into its genetic and environmental components.

Two alternative models are tested to describe how genetic and environmental factors may influence covariation. In the common pathway model, genetic and environmental factors influence covariation through a single common pathway. Such a model contains no separate genetic and environmental latent factors. Rather, genetic and environmental variables act conjointly through one or more latent phenotypes. By contrast, in the independent pathway model, genes and the environment can contribute to covariance through separate genetic and environmental latent factors.

Because we had only four subtypes of phobias to examine, only single-factor models were identified. It was not possible to test multifactor models, such as, for example, that animal and social phobias arise from an distinct evolutionary and neurobiologic mechanisms.

The form of data for our multivariate genetic analysis is two 8 × 8 tetrachoric correlation matrices, calculated by PRELIS, giving the tetrachoric correlations within and across twins for the four phobia subtypes, separately for MZ and DZ twins. To describe best how genes and environment influence the resemblance among the subtypes of phobias, the multivariate models were fitted to these matrices by means of LISREL by the method of weighted least squares. As in the univariate analysis of individual subtypes of phobias, the fit of the various models was compared by a χ² difference test, and the model that best combined the features of parsimony and goodness of fit was selected by Akaikes'44 information criterion (AIC).

The impact of mode of interview and zygosity (MZ vs DZ) on the risk of phobias was assessed by logistic regression in which the dependent variable was the presence vs absence of a diagnosis of phobia. In all such analyses, age was included as a control variable and the statistical significance of the independent variable was determined by a χ² test with 1 df. To test the “equal environment assumption” (ie, that MZ and DZ twins are equally correlated for exposure to the environmental experiences that are etiologically relevant for phobias), the impact of the similarity of childhood and adult environment on the similarity for phobias was assessed by logistic regression in which twin-pair similarity for phobias (concordant for affection or nonaffection vs discordant) was the dependent variable.

The difference in comorbidity in the different phobic subtypes was assessed by a log-linear model in CATMOD.3 Standardized life table curves (in which data for only affected individuals were analyzed, so that 100% of the sample eventually experienced onset) were obtained with the use of the LIFETEST procedure.3 Our analyses of age at onset, which was not available for all phobia subtypes in some twins, were based on the following sample size: agoraphobia, 33 twins; social phobia, 81 twins; animal phobia, 118 twins; and situational phobia, 96 twins.

RESULTS

Prevalence and Mode of Interview

Of the 2163 interviewed twins, 722 (33.4%) gave a lifetime history of any phobia, 654 of whom met criteria for one or more of the four specific phobic subtypes. Of the four subtypes, situational phobia was the most common (12.3%), followed by social phobia (11.5%), animal phobia (10.9%), and agoraphobia (8.7%). The lifetime prevalence of any simple phobia (animal or situational) was 20.2%. Of the twins suffering from one or more of the four subtypes, 443 (67.7%) met criteria for only one subtype, 149 (22.8%) met criteria for two, 51 (7.8%) met criteria for three, and 11 (1.7%) met criteria for all four specific phobias. The proportion of the total sample and the proportion of individuals meeting criteria for each subtype of phobia that endorsed the assessed specific unreasonable fears are seen in Table 1.

The mode of interview (phone vs face to face) was not significantly related to risk for any phobia or any specific subtype of phobia. Whether or not the cotwin agreed to be interviewed was also unrelated to risk for agoraphobia, social phobia, or situational phobia. The results for any phobia (χ² = 4.12, P = .04) and animal phobia (χ² = 5.35, P = .02), while significant, were in the opposite direction from that predicted (refusal in cotwin predicting lower risk for phobia).

Age at Onset, Structure of Phobias, and Comorbidity

The standardized onset curves for the four forms of phobia (Fig 1) were significantly different from one another (log-rank χ² = 30.10, df = 3, P < .0001). Onset was earliest for animal phobias, followed by situational phobia and social phobia. Onset was latest in agoraphobia.

The within-individual tetrachoric correlation matrix for the four phobias is seen in Table 2. All correlations were positive and in the range of +.30 except for the correlations between agoraphobia and social phobia (+.54) and between agoraphobia and
situational phobia (+.44). Factor analysis yielded a single meaningful factor on which agoraphobia had the highest loading (+.79), followed by social phobia and situational phobia.

The odds ratios of phobias with the other psychiatric disorders assessed at interview are seen in Table 3. For any phobia, the odds ratio was highest for panic disorder (8.83), followed by alcoholism (2.79) and eating disorders (2.62). The lowest odds ratios were found for major depression (2.26) and generalized anxiety disorder (2.16).

For all disorders except eating disorders, the odds ratio was highest for agoraphobia. For both panic disorder and major depression, the odds ratio for agoraphobia was significantly greater than for either animal or situational phobia. For generalized anxiety disorder and alcoholism, the odds ratio for agoraphobia significantly exceeded that for situational phobia. In general, the odds ratios for social phobia fell in between those found for agoraphobia and the simple phobias (animal and situational).

**Genetic Analyses**

**Testing the Equal Environment Assumption.**—The lifetime prevalence did not differ in MZ vs DZ twins for any phobia, or for social, animal, or situation phobia. The prevalence of agoraphobia, however, was significantly greater in DZ than in MZ twins ($\chi^2=5.76$, $P=.02$). Controlling for the effect of zygosity, the similarity of childhood environment did not predict similarity in members of a twin pair with respect to any phobia, agoraphobia, social phobia, or situational phobia. But it did predict a higher concordance in twin pairs for animal phobia ($\chi^2=5.09$, $P=.02$). Controlling for the effect of zygosity, the frequency of contact as adults did not predict similarity with respect to any phobia or to the four individual phobia subtypes.

**Probandwise Concordance and Univariate Twin Analyses.**—The lifetime prevalence, probandwise concordance, and tetra-chor correlation for any phobia and for the four phobia subtypes in MZ and DZ twins are shown in Table 4. The tetra-choric correlations in MZ twins ranged from +.27 (situational phobia) to +.41 (agoraphobia) (all $P<.01$). The correlations in DZ twins ranged from −.04 (animal phobia) to +.27 (situational phobia) and were, with the notable exception of situational phobia, much lower than the corresponding MZ correlations.

The results of model fitting to the twin data are seen in Table 5. For any phobia, the AE model, which posits that the disease liability results only from additive genetic (A) and individual-specific environmental (E) factors, provided the best fit, with heritability estimated at 32%. The AE model also provided the best fit for agoraphobia, social phobia, and animal phobia, with estimates of heritability between 30% and 39%. Despite the large sample examined in the report, however, only with animal phobias could the CE model, which postulates that disease liability results only from familial environmental (C) and individual-specific environmental (E) factors, be rejected as compared with the full ACE model by the rigorous $\chi^2$ difference test ($\chi^2=4.18$, $df=1$, $P<.05$).

The results of model fitting were quite different with situational phobia. Here, the CE model was the best fit, suggesting that 27% of the variance in liability to situational phobia is due to familial environmental factors. However, for situational phobia, the AE model, although producing a poorer general fit, could not be rejected by a $\chi^2$ difference test against the full ACE model.

**Multivariate Genetic Analysis.**—In these analyses, outlined in Table 6, we attempted to distinguish the effects of genetic and environmental etiologic factors that were common to all phobia subtypes from the effects of genetic and environmental factors...
Table 4.—Lifetime Prevalence, Probandwise Concordance, and Tetrachoric Correlations in MZ and DZ Twins for Any Phobia and Four Phobia Subtypes

<table>
<thead>
<tr>
<th>Phobia</th>
<th>MZ</th>
<th>DZ</th>
<th>MZ</th>
<th>DZ</th>
<th>MZ</th>
<th>DZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>30.0</td>
<td>31.2</td>
<td>41.9</td>
<td>37.0</td>
<td>.32</td>
<td>.15</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>7.3</td>
<td>10.3</td>
<td>23.2</td>
<td>15.3</td>
<td>.41</td>
<td>.15</td>
</tr>
<tr>
<td>Social phobia</td>
<td>11.7</td>
<td>11.6</td>
<td>24.4</td>
<td>15.3</td>
<td>.31</td>
<td>.12</td>
</tr>
<tr>
<td>Animal phobia</td>
<td>10.5</td>
<td>12.1</td>
<td>25.9</td>
<td>11.0</td>
<td>.38</td>
<td>.04</td>
</tr>
<tr>
<td>Situational phobia</td>
<td>11.6</td>
<td>12.9</td>
<td>22.2</td>
<td>23.7</td>
<td>.27</td>
<td>.27</td>
</tr>
</tbody>
</table>

*MZ indicates monozygotic; DZ, dizygotic.
†Corrected, by regression analysis, for small mean differences in age in MZ and DZ twins.

that were of etiologic importance only for specific subtypes of phobia. As with all our analyses, our goal was to find the most parsimonious model that provided a good explanation of the observed data. This was done by determining the model that produced the most negative value of the AIC.

We began with a full independent pathway model (see above and Kendler et al., especially their Figure, for further information about independent vs common pathway models) that included additive genetic, familial environmental, and individual-specific environmental factors both unique to each phobia and common to all four phobias. This model (model 1) fit very well ($x^2=33.3$, $df=48$, $P=.60$, AIC = -38.7). We then fit a common pathway model of the same type (ACE for both phobia specific factors and phobia common factors (model 2)), which produced a slightly less negative AIC than model 1 ($x^2=45.9$, $df=54$, AIC = -38.1).

In model 3, we eliminated from model 1 the familial environmental common factor and produced a modestly more negative AIC ($x^2=41.1$, $df=52$, AIC = -38.9). However, eliminating the additive genetic common factor from model 1 (model 4) produced a slight deterioration in the AIC ($x^2=41.7$, $df=52$, AIC = -38.3).

Eliminating phobia specific familial environmental factors from model 3 (model 5) substantially improved the fit ($x^2=42.4$, $df=56$, AIC = -45.6). Since the individual environmental factors specific to agoraphobia and the additive genetic factors specific to animal phobias were estimated at zero in model 5, in model 6 these were set to zero, producing the same fit, but two fewer $df$ and the best obtainable AIC value ($-49.6$).

The parameter estimates for the best-fitting model 6 are depicted in Fig 2. The additive genetic common phobia factor had the highest loading on animal phobias and the lowest on agoraphobia. The individual-specific environmental common phobia factor had the reverse pattern, with the highest loading on agoraphobia and the lowest on animal phobia. Comparing these loadings with those found in the standard (pheno)typic factor analysis (Table 2) suggested that most of the observed pattern of comorbidity between the subtypes of phobias results from the operation of environmental risk factors.

The sources of variance in liability to the individual phobias as determined by model 6 vary widely across the four phobia subtypes (Table 7). Specific genetic factors were more important than common genetic factors for all subtypes except animal phobia. Environmental risk factors specific for individual phobia subtypes were more important than environmental risk factors common to all phobias for all subtypes except agoraphobia. Social and situational phobias were similar in that about two thirds of the genetic variation was due to genes specific to the individual phobias. However, they differed in that for social phobia, common and specific environmental factors were about equally important, while for situational phobia, environmental factors

Table 5.—Fit of Twin Models and Parameter Estimates for Best-Fitting Model for Phobias

<table>
<thead>
<tr>
<th>Fit of Twin Model, $x^2$ Units</th>
<th>Parameter Estimates for Best-Fitting Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phobia</td>
<td>$a^2$</td>
</tr>
<tr>
<td>ACE</td>
<td>.03</td>
</tr>
<tr>
<td>CE</td>
<td>.06</td>
</tr>
<tr>
<td>AE</td>
<td>.10</td>
</tr>
<tr>
<td>Animal phobia</td>
<td>.29</td>
</tr>
<tr>
<td>Social phobia</td>
<td>.00</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>.04</td>
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<tr>
<td>Common</td>
<td>.06</td>
</tr>
<tr>
<td>Individual</td>
<td>.10</td>
</tr>
<tr>
<td>Specific</td>
<td>.29</td>
</tr>
</tbody>
</table>

*$A$ indicates additive genetic effects; $C$, common or familial environmental effects; $E$, individual-specific environmental effects; and $D$, dominance genetic effects. Thus, an ACE model includes additive genetic, common environmental, and individual-specific environmental risk factors; $a^2$ indicates proportion of variance in liability due to additive genetic factors (narrow heritability); $c^2$, proportion of variance in liability due to common or familial environmental effects; and $e^2$, proportion of variance in liability due to individual-specific environmental effects.

†The fit can be greater than zero with these models because all parameters are constrained to be greater than or equal to zero.

Table 6.—Results of Multivariate Model Fitting

<table>
<thead>
<tr>
<th>Model</th>
<th>Phobia Specific Factors</th>
<th>Phobia Common Factors</th>
<th>Pathway</th>
<th>$x^2$</th>
<th>$df$</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ACE</td>
<td>ACE</td>
<td>Independent</td>
<td>33.3</td>
<td>48</td>
<td>-38.7</td>
</tr>
<tr>
<td>2</td>
<td>ACE</td>
<td>ACE</td>
<td>Common</td>
<td>45.9</td>
<td>42</td>
<td>-38.1</td>
</tr>
<tr>
<td>3</td>
<td>ACE</td>
<td>AE</td>
<td>Independent</td>
<td>41.1</td>
<td>52</td>
<td>-38.9</td>
</tr>
<tr>
<td>4</td>
<td>ACE</td>
<td>CE</td>
<td>Independent</td>
<td>41.7</td>
<td>52</td>
<td>-38.3</td>
</tr>
<tr>
<td>5</td>
<td>AE</td>
<td>AE</td>
<td>Independent</td>
<td>42.4</td>
<td>56</td>
<td>-45.6</td>
</tr>
<tr>
<td>6†</td>
<td>AE</td>
<td>AE</td>
<td>Independent</td>
<td>42.4</td>
<td>56</td>
<td>-49.6</td>
</tr>
</tbody>
</table>

*A indicates additive genetic effects; $C$, common or familial environmental effects; $E$, individual-specific environmental effects; and $AIC$, Akaike's information criterion. Specific factors influence only each individual phobia subtype, while common factors influence all the phobia subtypes. See text and Kendler et al.** for an explanation of common vs independent pathway models.

†Best-fitting model by AIC.

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earlier in the animal than in the situational subtype. As in the Epidemiologic Catchment Area study, we found that age at onset of phobias was usually in childhood and adolescence. Our results also replicated previous findings that the rate of onset of social phobia is highest in the teenage years.

In accord with previous research, we found that the pattern of comorbidity differed substantially across the four subtypes of phobias; agoraphobia consistently had the highest rates of comorbidity, and animal and situational phobias had the lowest. As with age at onset, social phobias appeared, from the perspective of comorbidity, to fall between agoraphobia and animal and situational phobias.

### Univariate Twin Analyses

Prior to our twin analyses, we tested for potential confounding biases. The risk for any phobia and for three of the four specific phobias was unrelated to zygosity. However, MZ twins had significantly lower rates of agoraphobia than DZ twins, as was found, in this sample, for one of six definitions of generalized anxiety disorder. This difference might reflect a protective effect of the close emotional bond between MZ twins, an impact of agoraphobia on cooperation rates, or sibling interaction in which the predisposition to agoraphobia in one twin reduces the liability to agoraphobia in the cotwin. It is, however, difficult to see why these processes would affect only agoraphobia and not other phobias, alcohol dependence, or nearly all definitions of major depression, none of which have significant differences in prevalence in MZ vs DZ twins. Differences in base rates in the two zygozity groups have been incorporated into the analysis, as the tetrachoric correlations allow for different thresholds in MZ and DZ twins.

Similarity of childhood or adult environment was unrelated to twin resemblance for all except animal phobias. The relationship between similarity of childhood environment and concordance for animal phobia was, given the size of the sample, at a moderate level of statistical significance ($\chi^2 = 4.27, P = .04$) and could plausibly be the result of chance fluctuations. However, it could be a real effect of exposure to environmental stimuli in childhood, such as spiders, snakes, or frightening dogs, which would be more highly correlated in MZ than DZ twin girls because the former more often slept in the same room and played together. If real, this effect of environmental similarity could upwardly bias our estimates of the heritability of animal phobias. To test this, we matched MZ and DZ twins for similarity of childhood environment and then reapplied our twin models. The new estimate of the heritability of liability to animal phobias (30.5%) was only slightly less than that obtained above (32.5%), indicating that, if real, the greater similarity of childhood environment for MZ vs DZ twins did not substantially bias our results. In general, then, our findings support the validity of the "equal environment assumption" of the twin method with respect to the risk for phobias.

Consistent with previous family studies, we found that the liability to phobias was significantly correlated in twin pairs. Model fitting suggested that for any phobia, and for three of the four phobia subtypes, this familial aggregation was best explained solely by additive genetic factors. Estimates for the heritability, the proportion of total vari-
ance in disease liability due to genetic factors, ranged from 30% for social phobia to 39% for agoraphobia. Contrary to the two previous small-sample twin studies of phobia, where evidence of genetic effects only occurred when phobiclike fears or nonphobic anxiety disorder were considered, 25,26 we found evidence of the genetic transmission of clinically defined phobias. Although not trivial, the estimated heritabilities of liability to phobias were substantially lower than those previously reported from twin studies of bipolar illness and schizophrenia, where they have usually ranged from 60% to 90%. 30,31

However, for situational phobias, a qualitatively different result was obtained. Model fitting suggested that familial resemblance was the result solely of familial environmental influences. These results can be interpreted in two plausible ways. Either the causes of familial resemblance really differ for situational vs other forms of phobia and this is a true finding, or they do not differ and this finding results from random statistical fluctuation. We evaluated these two hypotheses in three ways. First, in the multivariate analysis, which, unlike the univariate analyses, includes the cross-twin cross-phobia correlations, the best-fitting model predicted that familial resemblance for situational phobia resulted only from genetic factors. Second, when we expanded our analyses to include, in a multiple threshold model, unreasonable situational fears without interference, the bivariate correlations in MZ twins substantially exceeded those in DZ twins, and model fitting predicted that familial resemblance for the liability to situational fears/phobias resulted solely from genetic factors. Third, we expanded the definition of situational phobia to include other simple, non-animal phobias, such as fear of water and thunderstorms. This change of definition modestly increased the number of twins with situational phobia, but the MZ and DZ twin bivariate correlations remained similar for both zygosity groups, and model fitting indicated that familial resemblance was still due entirely to familial environmental influences. Only a new sample will definitively address this question, although parsimony and our clinical intuition suggest that the second hypothesis is more plausible.

In summary, the results of univariate genetic analyses are consistent with predictions of the inherited phobia proneness model. If evolutionary fitness is maximized by a moderate degree of phobia proneness, our findings of modest additive genetic variance for the liability to phobias are as predicted by evolutionary theory. The estimated heritability of liability for phobias found in this sample indicates that genetic factors play a significant but by no means overwhelming role in the etiology of phobias. Individual-specific environment appears to account for approximately twice as much variance in liability to phobias as do genetic factors. Although some of this environmental variance may result from unreliability of measurement, our findings are also consistent with conditioning models of phobias in suggesting that individual-specific traumatic environmental experiences play a major role in the etiology of phobias.

With the possible exception of situational phobias, our results provide little support for the “social learning” model of phobias. If such a mechanism is etiologically important, it appears to occur in a small minority of cases, 20 or phobias are rarely “learned” from other family members. However, even with the large sample of twins examined in this report, our ability to discriminate between different models of familial transmission for the liability to phobias is limited. In the presence of moderate genetic influences, we have almost no power to detect additional modest familial environmental effects. 30 All that we can safely conclude is that, except perhaps for situational phobias, large familial environmental influences on individual phobias are unlikely.

**Multivariate Genetic Analysis**

We applied the method of multivariate genetic analysis to clarify the relationship of two kinds of genetic and environmental risk factors for the subtypes of phobia: those that are general, that influence risk for all phobia subtypes, and those that are specific, that influence risk to only one subtype of phobia. From a genetic perspective, this analysis examines the extent to which genes influence a general “phobia-proneness set-point” as opposed to specifically predisposing to only one phobia subtype. From an evolutionary perspective, we can ask: has evolution selected for a general predisposition to all phobic fears or only for the vulnerability to individual phobias? From an environmental perspective, these analyses will distinguish between environmental experiences that influence only the general phobia-proneness set-point vs those that influence risk to a single phobic subtype. Learning theory models of phobias would generally predict that most environmental risk factors for phobias would be subtype specific, as, for example, a traumatic exposure to a frightening animal would be unlikely to increase the risk for a public-speaking phobia.

In the initial stages of the multivariate analyses, the independent pathway model fit the data somewhat better than the common pathway model, suggesting that the genetic and environmental risk factors do not influence the pattern of the subtypes of phobias in the same way. Consistent with previous results from twin studies using self-report measures of fears, 15,18 we found strong evidence of the existence both of genetic and environmental risk factors unique to each kind of phobia and for genetic and environmental risk factors that influenced all phobia subtypes. Our results were midway between the two extreme hypotheses regarding the interrelationship of the subtypes of phobias: (1) the subtypes of phobias are distinct, unrelated syndromes and (2) the subtypes of phobia represent minor variations of a single disorder.

Klein 25 emphasized the major differences between agoraphobia and other phobic syndromes. A plausible prediction of this perspective is that agoraphobia should have the lowest loading on the phobia common factors. By contrast, in our phenotypic factor analysis (Table 3), agoraphobia had the highest loading of any phobia on the phobia common factor. Our multivariate genetic analysis indicated that the phenotypic structure was due almost entirely to the operation of environmental factors. While agoraphobia was most influenced by the environmental risk factors common to all phobias, it was least influenced by the genetic factors common to all phobias.

**General Implications**

Our results suggest that the subtypes of phobias can be placed along an etiologic continuum. At one end of this continuum lies agoraphobia, which has (1) the latest age at onset, (2) the highest rates of comorbidity, (3) the highest heritability, (4) the highest loading on the envi.
Environmetal common factor, (5) the least specific environmental influences, and (6) the lowest loading on the genetic common factor. At the other end of this continuum lye the simple phobias (animal and situational), which have (1) the earliest age at onset, (2) the lowest rates of comorbidity, (3) the lowest heritability, (4) the lowest loading on the environmental common factor, (5) the highest specific environmental influences, and (6) the (at least for animal phobias) highest loading on the common genetic factor. On nearly all of these measures, social phobia lies intermediate between agoraphobia and the simple phobias. Contrary to some previous research, our results suggest that situational phobias are more closely related to animal phobias than to agoraphobia.

Our results confirm the utility of the twin design for clarifying the nature of environmental risk factors. Consistent with previous research, we found that in the simple phobias, pathogenic environmental experiences are usually highly specific (e.g., being locked in a dark closet, bitten by a snake, nearly falling out of a window, etc.). The role of the environment in agoraphobia, by contrast, appears to be quite different, consisting of experiences that only influence the general level of phobia proneness.

Limitations

Our results should be interpreted in the context of six potentially significant limitations. First, these results apply only to women. Although no study has examined the sex-specific transmission of phobias, the substantial gender difference in prevalence suggests that genetic and environmental risk factors may differ in their impact on phobias in men and women.

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

Third, the lifetime prevalence rates for phobias in this sample are toward the high end of the range of those previously reported in women. Whether this is due to differences in populations or method is not clear. Our interviewer-based assessment of impairment, while more objective, may produce a lower “threshold” for interference than the self-report measure used in the Diagnostic Interview Schedule. This might explain the higher rates of phobias found in our compared with those obtained with the Diagnostic Interview Schedule in New Haven, Conn; St Louis, Mo; Puerto Rico; Edmonton, Alberta; and New Zealand. However, a lower threshold for interference should predict higher rates for all phobic subtypes. Compared with the national population estimates for white women from the Epidemiologic Catchment Area studies, however, our lifetime prevalence rate for agoraphobia was similar, whereas our rates for social and simple phobia were considerably higher. Furthermore, the lifetime prevalence rates of phobia were quite variable in the four Epidemiologic Catchment Area sites with comparable information. The rates found for any phobia in white women in Baltimore, Md, and the Piedmont (25.0% and 22.8%, respectively; W. Eaton, PhD, written communication, October 1990) are, in fact, only modestly lower than those reported here. Our prevalence rates of phobia may accurately reflect those found in the south-central Atlantic coast of the United States.

Fourth, a lifetime history of phobia was assessed in this study at a single point in time. Although the interrater reliability of our assessment was high, the test-retest reliability may be considerably lower. If uncorrelated in twin pairs, unreliability of measurement is indistinguishable from the effects of individual-specific environment in our twin models. If our twin models were “corrected” for the effect of unreliability, the estimates of the heritability of liability to phobias might be considerably higher than those reported here.

Finally, several times in our multivariate genetic analysis, one model was chosen over another on the basis of only slight statistical superiority. Therefore, some skepticism is indicated in acceptance of our final solution. Two alternative multivariate models fit the data nearly as well: a common pathway model, with a phobia general factor influenced by genes and individual-specific environment, and an independent pathway model, with familial and individual-specific environmental common factors.

Finally, the results presented herein are in several ways incomplete. We plan in the future to examine the following, from a genetic and epidemiologic perspective: (1) the relationship between phobias and unreasonable fears, (2) the interrelationship of phobias, panic, and generalized anxiety disorders, (3) the relationship between blood-injury phobias (being assessed at a follow-up interview) and the other phobic subtypes, (4) possible precursors for phobic disorders, including personality, social class, rearing experiences, and premature parental loss, and (5) the nature of parent-offspring transmission of the predisposition to phobias.

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