Genetics of Blood-Injury Fears and Phobias: A Population-Based Twin Study


Data on unreasonable fears of blood, needles, hospitals, and illness (BNHI) were collected by telephone interview from 541 MZ and 388 DZ pairs of female twins from the population-based Virginia Twin Registry. BNHI phobia was defined as the presence of fear accompanied by interference. Age at onset of phobia was found to be very similar to that of situational phobias previously assessed in the sample. Using a multiple threshold model, we found no evidence for qualitative differences between BNHI fears and BNHI phobia. The familial aggregation of fears appears to be entirely due to additive genetic variance. The possible exception to this is fear of illness, which, like BNHI phobias, seems to aggregate within families because of shared environmental factors. Although power to discriminate between the causes of familial resemblance is low, results suggest that random traumatic events and some social learning may be responsible for the onset of BNHI phobias. About two-thirds of variance is individual-specific environmental, and could include genotype × environment interaction and measurement error. © 1994 Wiley-Liss, Inc.

KEY WORDS: fears, phobias, blood, injury, hospital, needles, twins, genetics, age at onset, mx

INTRODUCTION

Fear is a normal reaction to a dangerous situation or object, and has obvious survival value. A phobia is a fear out of proportion to the actual danger of the stimulus, which cannot be reasoned away. Clinically, we define phobias as unreasonable fears of sufficient intensity to interfere with normal behavior [4]. Fear is thus a necessary, but not sufficient, condition for phobia. One explanation of phobias is that they are simply extreme fears. Alternatively, additional factors may be necessary for the development of a phobia.

Mild fear of blood is common in children from ages of six or less [24], and declines with age. Extreme fear is much less frequent, but persists to adulthood in about 2-3% of the population, and is therefore one of the most common adult phobias [1, 31, 54]. Phobias of blood, venipuncture, medical procedures, and illness are classed as simple [4]. Like other phobias, its etiology remains unclear, though theories abound.

As described in an earlier article [21], there are three broad types of model for phobia. First, the chance association of fear-inducing and innocuous stimuli could associate a fear response with the benign stimulus through classical conditioning [52, 29, 42, 15]. Second, fears may be learned from others—particularly parents—which we call modeling. Third, there could be some inherited predisposition to acquire phobias. Two varieties of this model are (i) preparedness to develop conditional responses and (ii) innate fear which requires no learning. Both models typically incorporate genetic factors which generate the biological predisposition to develop phobias.

These models have distinct predictions for the genetic-environmental architecture of extreme fear. First, the accidental co-occurrence of stimulus and fear response would seem to offer little role for genetic factors and would perhaps show little familial aggregation whatsoever. Second, modeling phobic responses on others would implicate environmental factors; these may or may not be shared by members of a family. Third, some biological preparedness to develop extreme fears suggests the possibility of genetic variation and perhaps genotype × environmental interaction. Finally, innate fears suggest a strong role for genetic factors. In this article, we shall review the literature on the genetics of blood-injury phobias and supplement it with new data from the Virginia Twin Registry.

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GENETIC STUDIES OF BLOOD-INJURY FEARS AND PHOBIAS

Support for the hypothesis that genetic factors contribute to variation in fears has been consistent across a variety of studies, both animal and human [9, 29, Ch. 6]. Common fears generally show the same pattern of inheritance as personality [45, 32, 40], and two studies of blood-injury fears reveal similar findings. In data on the Fear Survey Schedule II [17] collected from a (N = 250 pairs) volunteer twin sample [45], the morbid fears factor, which includes items about blood, needles, injury, the dark, closed places, and cemeteries, correlates .46 in MZ and .24 in DZ twins [32]. In contrast to personality, however, there is some evidence for marital resemblance (r = .20; P < .001). Several studies report greater familial resemblance for fears and phobias of blood-injury than for other stimuli [27, 28, 10, 54, 47], but this was not supported by the twin data collected by Rose et al. [45].

Torgerson’s twin study produced somewhat similar results. Although MZ correlations for blood-injury fears were greater than those found for DZ twins, once again there was no evidence that this type of fear was more familial than any other. Its small size and unusual sample structure may account for the fact that MZ and DZ twin correlations for blood-injury fears were lower than simple, animal, and social ones. Furthermore, the MZ and DZ correlations of .35 and −.20, respectively, are not consistent with a simple genetic model. The study was conducted with a sample that was partly (11 pairs) twins discordant for hospitalization for neurotic disorder, and partly (88 pairs) from a “relatively unselected” sample. The need for replication with a population-based or systematically ascertained sample is thus acute.

Genetically informative studies of clinically-defined phobias have been rare, and the two known to us are relatively uninformative because of their small sample size. Both used clinically ascertained samples. Carey and Gottesman [56] reported low and similar concordance rates among the MZ and DZ cotwins for phobic disorder, although some evidence of genetic etiology was found when a broader definition of phobia was used. Similarly, Torgersen [49] found that of 12 twin probands hospitalized with a primary diagnosis of phobia, none had a phobic cotwin. Thus most studies of blood-injury phobia to date have suffered from problems of nonrandom sampling and small sample size, and none has examined the critical equal environments assumption (EEA) of the classical twin study [22]. The assumption is that the environments of MZ twins are no more similar than those of DZ twins for characteristics that cause variation in the phenotype under study.

In addition to these studies of the genetics of fears and phobias, there are data which indirectly support the notion of genetic preparedness. Neurophysiological studies in both humans and animals implicate fear in behavioral regulation, which is thought to be reflected in measures of personality [18]. Psychophysiological measures, such as EEG responses and skin conductance, typically show a high proportion of genetic variance [25, 26]. Phenotypic variance in personality is typically 40–50% additive, plus nonadditive genetic, and the remainder specific environment, with little assortative mating [13]. If fearfulness is related to neurochemistry and personality, some genetic variance would seem likely.

Studies of other types of phobia may suggest genetic variance for blood-injury phobia. Our earlier personal interview studies of social, situational, simple, and agoraphobia in adult female MZ and DZ twins [21] showed modest familial aggregation consistent with a model of additive genetic and random environmental sources, with no role for the shared or family environment. If the same broad theory of phobic response applies to all types of phobia, then blood-injury phobia should be no exception. We did not assess blood, needle, hospital, or illness phobias during the personal interview study described above. This was corrected during telephone interviews which took place some 17 mo after the personal interview. The data were collected in a way that allows us to analyze either phobia or fear as separate endpoints.

Data collected from pairs of relatives offer a means of testing the normality of the underlying distribution of liability. Using a multiple threshold model [43, 34], we can test whether the pattern of fears and phobias in twin pairs is consistent with the hypothesis that phobia simply represents an extreme score on a normal distribution of liability to fear. This test is implicit when we fit models to contingency tables based on categories, such as no fear, fear but no interference, mild interference, and major interference. Further exploration of the covariance structure may be obtained by grouping these categories together, and comparing the twin resemblance in $2 \times 2$ tables of fear vs. no fear with tables of no interference vs. interference.

UNUSUAL CHARACTERISTICS OF BLOOD-INJURY PHOBIAS

Blood phobic response shows a distinct cardiovascular reaction. Initially, there is a slight increase in heart rate and blood pressure, just as there is with other phobias. However, this temporary elevation is followed by marked slowing of the heart rate [38] which develops over several minutes and may even lead to asystole [29]. Fainting can be common at either the sight or mention of the phobic stimulus [38, 29, 50]. These responses are peculiar to the blood phobic; other types of phobic patient do not generally react in this way [10]. On the contrary, other phobias are usually accompanied by an increase in blood pressure and heart rate. Another feature that distinguishes blood-injury phobia from others is that less fear per se is reported; nausea and faintness tend to predominate.

Despite these differences, blood-injury phobias are quite similar to animal or simple phobias in terms of their age at onset and course. They also respond very similarly to treatment through exposure, although some additional considerations may be necessary to avert fainting and other unpleasant sequelae of bradycardia [29]. It is less clear whether fear of illness should be grouped with fear of blood, injury, needles, and the
like. Sometimes illness fears may arise as a result of blood-injury fearfulness. Other forms, such as fear of AIDS, seem focused on the illness itself and lack the bradycardic response of the blood-injury phobic [51]. We will use our twin data to test, as far as possible, the validity of this distinction.

GOALS

There are six main goals of this paper. We aim to: (i) report epidemiologic data on the prevalence, age at onset, and comorbidity of BHNI phobias; (ii) fit models of genetic, shared, and specific environmental factors to twin data on BHNI fears; (iii) do the same for BHNI phobias; (iv) examine the EEA for phobias; (v) examine the relationship between BHNI fears and phobias by testing the fit of a multiple threshold model; and (vi) compare these results to those for other phobias reported in an earlier article.

SUBJECTS AND METHODS

The sample and our general approach to the analysis of population-based twin data have been described in detail elsewhere [20]. In brief, this sample of Caucasian female same-sex twins was obtained from the population-based Virginia Twin Register, formed from a systematic review of birth records in the Commonwealth of Virginia. Twins were eligible to participate if both members of the pair had previously responded to a mailed questionnaire. At what we call time-1, we succeeded in personally interviewing 2,163 (92.0%) of the 2,352 eligible individuals, which yielded 1,033 pairs with both twins interviewed. Of the completed time-1 interviews, 89.3% were performed face to face and 10.7% by telephone. Interviews were conducted by trained social workers, blind to the status of the cotwin. Zygosity was determined blindly by standard questions [13], photographs, and, when necessary, DNA [46]. Attempts were made to recontact all 2,163 originally interviewed twins a minimum of one yr after their time-1 interview. We succeeded in completing time-2 personal interviews with 2,001 (92.5%) of them, including both members of 938 pairs, the zygosity assignment of which were 546 MZ, 390 DZ, and 2 pairs of unknown zygosity.

Unlike the time-1 interviews, nearly all of the time-2 interviews (98.6%) were completed by phone. The average number of months (±SD) between the time-1 and time-2 interviews was 17.3 ± 3.8. With the goal of increasing cooperation, where possible the same interviewer completed the interview at both times. However, because of changes in personnel, this was not possible for a substantial proportion of the twins. Interviewers did not review time-1 interviews prior to time-2 interviews. If they recalled information from the time-1 interview, they were instructed not to mention this during the time-2 interview, nor to let it bias their scoring of that interview. The time-2 interviews were also conducted blind to knowledge of the psychopathologic status of the cotwin. Time-1 data on phobias and other psychopathology are used for comparison with the BNHI data collected at time-2.

Lifetime prevalence of fears and phobias was assessed by an adaptation of the Phobic Disorders section of the Diagnostic Interview Schedule Version III-A [44], which in turn was based on the DSM III criteria [4]. Collection of data at the time-1 personal interview has been described in detail elsewhere [21]. Only BNHI fears were investigated at time-2. First, twins were asked whether or not they had an unreasonable fear of each of: (i) blood; (ii) needles; (iii) hospitals; and (iv) illness. In common with the earlier assessments, our interviewers were trained to assess whether the unreasonable fear had significant objective behavioral impact on the respondents' life. This assessment was made for the four phobic stimuli jointly. Thus, individuals could belong to one of four categories: no fear, fear without interference, fear with minor interference, and fear with major interference. Examples of minor interference would include not watching movies with violence, or putting off doctor's appointments for minor ailments. Major interference would involve severe problems with major life functions, such as occupation or place of residence, or refusal to go to the hospital for serious medical problems. Of the 414 subjects who reported such fears, 29.9% were judged to have minor or major interference.

Blood-needle-hospital-illness (BNHI) phobia was defined in this report as fear that the respondent recognized as unreasonable and which was, in the judgment of the interviewer, accompanied by minor or major interference. If the subject indicated more than one unreasonable fear, we did not record which of the stimuli led to interference. Despite this methodological shortcoming, we were able to identify "pure" illness phobics whose only unreasonable fear (of the four) was illness, and who suffered interference from it. Thus, because of the uncertainty noted above, we distinguish between blood-injury phobia with vs. without illness. We refer to these as BNHI and BNH, respectively.

We have no data on inter-rater reliability for the telephone interviews made at time-2. However, no difference has been found between personal and telephone interviews made at time-1, and very high inter-rater agreement was found for other phobias assessed at that time [21]. It seems likely that the reliability of assessment of blood-injury phobias, with their dramatic fainting responses, would be at least as good as that of other phobic disorders.

To assess possible violations of the EEA, twins were asked at time-1 the frequency with which they saw or had contact with their cotwin, with responses ranging from every day to once a year or less. Similarly, subjective reports of how similarly the twins were treated as children were made.

Statistical Analysis

As outlined previously [20], probandwise concordance is an appropriate summary statistic for twin studies when affected individuals have been ascertained through treatment facilities. However, when examining a general population twin sample, probandwise concordance is very inefficient because it ignores twins concordant for nonaffectation. Therefore, we use Mx [33] to fit models directly to the contingency tables by maximum likelihood. The method is based on the
polychoric correlation [34] (or “correlation of liability” [16]). For a given set of parameter estimates, the software uses the structural equation model to derive predicted MZ and DZ twin correlations. For each group, the program computes the proportions expected under different parts of the bivariate normal distribution, which vary according to the estimates of the population threshold and the correlation in liability. The expected proportions are multiplied by the number of pairs in that group to compute expected cell frequencies. The log-likelihood of the observed frequencies given the model parameters is then calculated for each group and summed. Note that for contingency tables larger than $2 \times 2$, the overall goodness of fit of the model reflects how well the bivariate normal model is able to reproduce the observed pattern of cell frequencies [34], as well as how well the hypothesized genetic model fits the pattern of twin correlations.

Our genetic models postulate three sources of variance in liability to phobia: (i) additive genetic effects (A), (ii) shared family or “common” environment (C), and (iii) individual-specific environment (E). The effects of genetic dominance are confounded with those of the shared environment in this sample. The proportion of total variance in liability due to additive genetic effects and common and individual-specific environment are termed, respectively, $a^2, c^2$ and $e^2$. As a general fit index for our models, we used Akaike's information criterion [3, AIC], calculated as $\chi^2$ minus twice the degrees of freedom (d.f.), which reflects both the goodness of fit and parsimony of the model. The more negative the value of the AIC, the better the overall fit of the model relative to the number of estimated parameters. Degrees of freedom equals the number cells minus one for each contingency table, less the number of free parameters estimated, plus one recovered by the constraint that $a^2 + c^2 + e^2 = 1$. For example, in the $4 \times 4$ table case it is $16 - 1$ cells for each of the MZ and DZ groups, less 3 thresholds and 3 parameters, plus one for the constraint, equals $30 - 6 - 1 + 25$. Note that thresholds were equated for twin 1 and twin 2 across MZ and DZ twins. Marked differences in thresholds between MZ and DZ twins would indicate failure of the model and would be reflected by a poor fit of the model.

Where appropriate, we also report a $\chi^2$ difference test (a likelihood ratio test) between a model and a submodel, where the degrees of freedom represent the number of parameters in the model that are fixed in the submodel.

RESULTS

Prevalence, Age at Onset, and Comorbidity

Table I shows the contingency tables of the fear/phobia category of pairs of MZ and DZ twins. It also shows summary statistics from these tables, giving the percentage in each category, both separately for MZ and DZ twins, and for the whole sample. The higher rates of fears and phobias in DZ twins is almost statistically significant ($\chi^2 = 7.61, P = .054$). The rate of BNHI phobia, defined as fear with minor or major interference, is 62/1,000. Eleven of the 124 phobics reported fear of illness only.

Figure 1 shows the proportion of phobics who had onset by a given age, for the BNHI data at time-2. This curve is shown together with the cumulative ages at onset of other phobias, as assessed at time-1, and as reported previously [21]. Onset of BNHI phobia is later than animal phobia, but earlier than agoraphobia, and almost identical to that of situational phobia.

Table II shows the odds ratios for lifetime risk of other major psychiatric disorders for both BNHI and BNH phobias. As would be expected for the relatively small number of phobics in each category (51 with BNH and 11 with illness only), no significant differences in rate were found. Nevertheless, these data may prove useful for meta-analysis. The greatest increases in risk are for alcoholism and animal phobias. The additional risk to other phobia subtypes may be expressed as correlation coefficients. BNHI phobia correlates .36, .33, .31, and .25 with agoraphobia, social phobia, animal phobia, and situational phobia respectively. Exploration of the comorbidity between phobias and other forms of psychiatric illness requires simultaneous multivariate genetic analysis of all disorders, which is described in another article [23].

Genetic Analysis

Univariate analysis of phobia. The data in Table I may be collapsed to $2 \times 2$ contingency tables according to the presence or absence of interference, our operational definition of phobia. We used Mx [33] to compute estimates of the tetrachoric correlations. The MZ and DZ correlations for BNHI phobia were .326 and .318, respectively. For BNH phobia, the corresponding correlations were .302 (MZ) and .287 (DZ). Table III shows the results of using Mx to fit, by maximum likelihood, a simple model of additive genetic, shared, and random environmental factors to these phobia data. Results are shown separately for including and excluding illness phobics. In both cases there is evidence for significant familial resemblance, but very little power to discern whether this is due to genetic or shared environmental factors. The only model rejected is that of no familial resemblance (E only). As would be expected from the observed correlations, the common and random environment model gives a practically perfect fit to the data. By Akaike's criterion, we would select the CE model as the most parsimonious explanation for the data for both definitions. However, the additive genetic and random environment model still fit well ($\chi^2 = 5.12; P = .28$ and $\chi^2 = 3.17; P = .53$). With such a small difference in fit between models, it is not possible to choose between them.

Univariate analysis of fears. Our BNHI data comprises questions about fear of blood, needles, hospitals, and disease, and the interference of these fears. Table IV shows the results of fitting simple genetic models to each item separately. For all four items, the model of no familial resemblance (E) fails. We find similar patterns of correlations for fears of blood (MZ: .59; DZ: .08), needles (MZ: .49; DZ: .10), and hospitals (MZ: .32; DZ: .16), to which a model of additive genetic and random environment gives (by AIC) the most parsimonious fit. However, for fear of illness (MZ: .26; DZ: .32),
TABLE I. Contingency Tables and Prevalences of MZ and DZ Twins

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Fear</th>
<th>Minor</th>
<th>Major</th>
<th>None</th>
<th>Fear</th>
<th>Minor</th>
<th>Major</th>
</tr>
</thead>
<tbody>
<tr>
<td>MZ twins n = 541</td>
<td>371</td>
<td>54</td>
<td>10</td>
<td>1</td>
<td>240</td>
<td>51</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>DZ twins n = 388</td>
<td>19</td>
<td>17</td>
<td>5</td>
<td>1</td>
<td>8</td>
<td>11</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>%</td>
<td>80.4</td>
<td>15.0</td>
<td>3.5</td>
<td>1.1</td>
<td>75.3</td>
<td>17.0</td>
<td>5.1</td>
<td>2.6</td>
</tr>
<tr>
<td>Whole sample, MZ &amp; DZ</td>
<td>78.3</td>
<td>15.8</td>
<td>4.2</td>
<td>1.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a model of shared environment and random environment is most parsimonious. Table IV also shows the results of fitting models to the fear scale, scored 0 (no fear) to 3 (fear with major interference). Two versions of the scale were used, according to whether those with fear of illness alone were counted as having fear. In both cases, the model of no familial resemblance (E) is strongly rejected. The data support the hypothesis that familial resemblance is genetic (AE) better than the hypothesis that it is environmental (CE). Again, the difference in fit between these models is not great.

**Equal environment assumption.** To test for the effects of similarity of treatment and frequency of contact, we divided the MZ and DZ twin groups into two groups each, according to whether they were above or below the entire sample median for the measure in question. We then fit a model incorporating a specified shared environment component to the four-group data. Details of this method can be found in Kendler et al. [22]. For both fear as an ordinal scale, and for phobia diagnoses, similarity of treatment did not significantly increase twin concordance (Phobia: χ² = 0.00; P = 1.0; Fear: χ² = 3.30; P = .07). Likewise, there was no significant effect of contact (Phobia: χ² = 0.26; P = .61; Fear: χ² = 0.98; P = .32). These components were dropped from subsequent model-fitting analyses and the data were summarized as two groups (MZ & DZ) to keep cell frequencies as high as possible.

**Phobia as part of the fear continuum.** When we treated the four categories (no fear, fear with no interference, fear with minor interference, and fear with major interference) as ordered responses on a normally distributed continuum of liability, the fit of the model was very good for both MZ (χ² = 6.051; P = .642) and DZ twins (χ² = 6.844; P = .554). However, the observed cell frequencies are low in several cases, which can create two problems: (i) lack of statistical power to reject the bivariate normal model; and (ii) slow asymptote of the maximum likelihood statistic to true χ² [2]. Thus these results should be interpreted with caution.

**COMMENT**

**Prevalence, Onset, and Comorbidity**

The prevalence of BNHI phobia found here is somewhat higher than that found in other studies of blood-injury phobia [1, 47]. By counting minor interference as phobic disorder, we may have a lower threshold for phobic disorder than in other studies. However, this study is one of relatively few that have examined blood-injury-illness phobia from an epidemiologic standpoint. We are unaware of any report concerning this phobia subtype from the Epidemiologic Catchment Area study (ECA) [7].

In agreement with other studies [37, 47], we found the onset of blood-injury phobia to be almost as early as that of animal phobia, and practically identical to that of situational phobia. Situational phobias, which include claustrophobia and acrophobia, would not seem to be directly related to blood or injury, but they do pose a physical threat from suffocation or falling. This threat seems greater than those of going out of the house alone, meeting new people, or mice, for example.

By merging the telephone interview data with those collected by personal interview approximately 14 mo previously, we found that, compared to the general population, blood-injury phobics suffer significantly increased risk for all forms of psychiatric illness except generalized anxiety disorder. The additional risks are greatest for alcoholism, eating disorders, and other phobias, and are not significantly different between those with illness phobia and those with blood-injury phobia. The level and pattern of risks resembles those

![Figure 1](attachment:image.png)  
Fig. 1. Cumulative age at onset curves for animal phobia, situational phobia, social phobia, agoraphobia, and BNHI phobia. The curves are standardized to asymptote at unity.
TABLE II. Odds Ratios (OR) for Lifetime Comorbidity Between Blood Phobia (n = 24), Blood Phobia Without Illness (n = 113), and Illness Phobia (n = 11) With Other Psychiatric Disorders

<table>
<thead>
<tr>
<th></th>
<th>Blood w/o illness</th>
<th>Illness</th>
<th>Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR 95% C.I.</td>
<td>OR 95% C.I.</td>
<td>OR 95% C.I.</td>
</tr>
<tr>
<td>MDD</td>
<td>1.89 1.28–2.78</td>
<td>1.29 0.37–4.43</td>
<td>1.82 1.26–2.63</td>
</tr>
<tr>
<td>Bulimia</td>
<td>2.87 1.61–5.13</td>
<td>1.86 0.25–14.75</td>
<td>2.78 1.58–4.89</td>
</tr>
<tr>
<td>Alcohol</td>
<td>3.04 1.70–5.45</td>
<td>11.23 3.23–39.05</td>
<td>3.68 2.10–6.09</td>
</tr>
<tr>
<td>Panic</td>
<td>1.78 0.79–3.98</td>
<td>5.92 1.25–27.92</td>
<td>2.10 1.02–4.31</td>
</tr>
<tr>
<td>GAD</td>
<td>1.45 0.71–2.96</td>
<td>1.65 0.21–12.81</td>
<td>1.47 0.74–2.90</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>2.84 1.73–4.66</td>
<td>9.71 2.92–32.24</td>
<td>3.27 2.07–5.17</td>
</tr>
<tr>
<td>Social phobia</td>
<td>2.88 1.83–4.52</td>
<td>7.19 2.18–23.76</td>
<td>3.16 2.07–4.83</td>
</tr>
<tr>
<td>Animal phobia</td>
<td>4.08 2.65–6.27</td>
<td>2.08 0.44–9.65</td>
<td>3.88 2.56–8.88</td>
</tr>
<tr>
<td>Acrophobia</td>
<td>2.47 1.58–3.87</td>
<td>1.65 0.35–7.68</td>
<td>2.40 1.55–3.71</td>
</tr>
<tr>
<td>Any phobia</td>
<td>3.22 2.19–4.74</td>
<td>6.67 1.76–25.20</td>
<td>3.42 2.36–4.96</td>
</tr>
</tbody>
</table>

\( \chi^2 \) is a test of homogeneity of odds ratios between those with and those without fear of illness.

The genetics of blood-injury fears and phobias

Our item analyses of specific fears implicate genetic factors in the etiology of fears of blood and needles. Fear of hospitals also shows a genetic pattern of twin correlations, but rates are too low to discriminate effectively between social environment and genetic factors as explanations for familial resemblance. MZ and DZ correlations are almost equal for fear of illness, though again these are rare enough in our sample that a genetic model of resemblance cannot be rejected. However, it seems quite possible that the characterization of blood-injury phobias as extreme squeamishness and illness phobias as hypochondriasis [27] has some basis.

The interview protocol assessed whether the four fears (blood, needles, hospitals, and illness) jointly led to major or minor interference with their lives, and this was used to operationalize the definition of phobia. Quite different results emerged from the analysis of the four-point fear scale from those found for phobia. While the former recaptured the additive genetic plus random environment pattern evident in most of the constituent fears, the latter did not. Instead, for blood-injury phobia with or without illness, the pattern of correlations was more consistent with a shared plus random environment model. We emphasize that this finding is based on relatively small numbers of phobics, and that the genetic model also gives a very good fit to the data. If replicated in a larger sample, the results would lend support to the hypothesis that blood-injury phobias—as opposed to extreme fears—develop according to some combination of classical conditioning of chance events and learning from others. In this context, we note that the classical conditioning arises from random and infrequent events, which are not likely to be shared by twins. Susceptibility to classical conditioning may have substantial genetic variance [14], which would appear if twins shared similar conditioning events. If there is substantial shared environment variance for interference, several explanations are plausible. Some parental rearing style might give rise to different strategies for dealing with fears—whether one allows them to interfere or not. Twin concordance for geographical residence might lead to between-pair variance for exposure to fear stimuli. However, the evidence here is weak and does not warrant further speculation.

Interestingly, the genetic architecture of blood-injury phobia is very similar to that of situational phobias in this sample [21], adding to the similarity in onset noted above. It may be that the presence or absence of these fears is partly genetic, while their development into phobias is influenced by environmental factors. We

TABLE III. Parameter Estimates and Goodness-of-Fit of Genetic Models for BNH Phobia and BNH Phobia

<table>
<thead>
<tr>
<th></th>
<th>BNH phobia</th>
<th>BNH phobia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ACE CE AE E</td>
<td>ACE CE AE E</td>
</tr>
<tr>
<td>A2</td>
<td>.049</td>
<td>.057</td>
</tr>
<tr>
<td>C2</td>
<td>.257</td>
<td>.278</td>
</tr>
<tr>
<td>E2</td>
<td>.794</td>
<td>.664</td>
</tr>
<tr>
<td>X2</td>
<td>2.62</td>
<td>4.39</td>
</tr>
<tr>
<td>AIC*</td>
<td>-3.38</td>
<td>-1.61</td>
</tr>
</tbody>
</table>

\( A = \text{additive genetic}; C = \text{common environment}; E = \text{random environment}. \)

\( X^2 \) is the chi-square statistic.

\( AIC \) is Akaike's Information Criterion.

Degrees of freedom: ACE, 3; AE or CE, 4; E, 5.
<table>
<thead>
<tr>
<th>Fear of blood</th>
<th>Fear of needles</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACE</strong></td>
<td><strong>CE</strong></td>
</tr>
<tr>
<td>$A^2$</td>
<td>.561</td>
</tr>
<tr>
<td>$C^2$</td>
<td>.000</td>
</tr>
<tr>
<td>$E^2$</td>
<td>.439</td>
</tr>
<tr>
<td>$x^2$</td>
<td>1.28</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fear of hospitals</th>
<th>Fear of disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACE</strong></td>
<td><strong>CE</strong></td>
</tr>
<tr>
<td>$A^2$</td>
<td>.343</td>
</tr>
<tr>
<td>$C^2$</td>
<td>.000</td>
</tr>
<tr>
<td>$E^2$</td>
<td>.657</td>
</tr>
<tr>
<td>$x^2$</td>
<td>6.10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fear scale (0-3)</th>
<th>Fear scale (0-3) w/o illness</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACE</strong></td>
<td><strong>CE</strong></td>
</tr>
<tr>
<td>$A^2$</td>
<td>.421</td>
</tr>
<tr>
<td>$C^2$</td>
<td>.000</td>
</tr>
<tr>
<td>$E^2$</td>
<td>.579</td>
</tr>
<tr>
<td>$x^2$</td>
<td>29.94</td>
</tr>
</tbody>
</table>

* Degrees of freedom: ACE, 3; CE or AE, 4; E, 5.
* Degrees of freedom: ACE, 26; AE or CE, 26; E, 27.

found no evidence for greater familial resemblance of BNHI or BNH phobia than for other phobias. It may be that subjects can assess BNH phobia in their relatives more accurately than other phobias, because of its dramatic cardiovascular response. Thus positive family history obtained by asking the proband about their relatives may yield artificially low rates for other phobias.

Ost (1991) reported that 54% of a sample of 136 blood or injection phobics attributed onset to conditioning experiences and a further 24% recalled vicarious experiences, though no such “priming” was reported by some 16% of the sample. Although there may be problems with recall of etiological factors in psychiatric disorders [35], these data seem consistent with our genetic analysis. The majority of such conditioning experiences would appear to be specific to the individual and not based on modeling of parental behavior, for example.

**Test of the Equal Environments Assumption**

No significant effect of either similarity of treatment or amount of contact was found for BNHI fears or phobias. However, for fears, the effect of treatment approaches significance. This is not too unlikely a finding given the number of tests reported both here and in other reports of this sample. Similar findings in other samples might prove significant in a meta-analysis. Such a finding would not necessarily invalidate the results of this study, because similar treatment might well be elicited by, rather than imposed upon, twins.

**Phobia as an Extreme Fear**

We found that the observed contingency tables did not reject the model of a single liability dimension underlying the continuum of no fear, fear without interference, fear with minor interference, and fear with major interference. However, this finding only provides weak support for the model because the statistical power to reject it is low (see Appendix). Even if liability to phobia was entirely independent of level of fearfulness, we would be unlikely to find evidence of this with our sample of 920 pairs.

**Etiology**

The resemblance of blood-injury phobia to situational phobia, in terms of age at onset and genetic architecture, is striking, but might be due to chance. Among blood-injury phobics, there is an increased risk of situational phobia, but this increase is no greater than for any other phobia subtype. It could be that there is some negative feedback between similar phobias; expression of one suppresses the other. In principle, we might expect those expressing both types to be less severely affected than if there was no such suppression effect, but the sample size required to test this hypothesis would be large.

**Limitations**

All subjects in this study are female, and therefore the results may not generalize to males. Some differences are to be expected because females have been found to have higher rates of phobic disorder in most [12, 1, 19, 53, 41, 8, 5]—but not all [36]—studies. We aim to collect data from male and male-female pairs in the second wave of our current study (MH-49492).

Although the Virginia Twin Registry is based on a comprehensive search of birth records, there is the possibility that the final sample of twins is not representative. They were selected for: (i) not moving out of state,
and (ii) prior response to questionnaire and interview surveys.

The lifetime rates of blood-injury phobias are rather higher in this study than in two others [1, 11], which might be due to our interpretation of “minor interference.” However, neither of these studies used DSM-III criteria to define phobia, and relatively few reports distinguish blood-injury phobia from other subtype. It is possible that there is a genuine demographic difference in the prevalence of fears in Virginia. The somewhat high rate of other phobias in this sample [21] is close to that found in Eastern US cities in the ECA study [6].

Though we tested the equal environment assumption with our data, it is possible that we have not assessed the critical aspects of similarity of treatment. Although more similar environmental conditions for MZ twins might explain their greater resemblance, it is important to distinguish between environmental conditions that are imposed on the twins externally, and those that they elicit. Such elicitation, if based on the phenotype of the twins, may indeed create more similar environments, but is correctly ascribed as genetic variance. It is simply that the genes act through their effects on the behavior of others [35].

We were not able to assess the test-retest reliability of the fear/phobia measures. This would be an important additional step, because low familial resemblance may be due to the unreliability of the measures. Unreliability of the measures would also reduce correlations with putative risk factors and sequelae of fear or phobia. The lower limit of reliability of the fear items is greater than that of the phobias, because they correlate more highly between twins. Nevertheless, with a maximum correlation of .59 for fear of blood in MZ twins, there is still room for considerable unreliability. Mode of interview (telephone vs. face-to-face) does not seem to be a major factor in the assessment of fears and phobias, because no discernable differences in rates could be found according to interview method in the first wave [21]. It is possible—though unlikely—that decreased specificity of the phone interview, for example, was counterbalanced by increased sensitivity, and thus equivalent rates were observed in the two interview methods.

Any experiment or observational study has limited power. The power of the classical twin study to discern genetic and environmental effects has been studied for quantitative variables [30]. Two factors seriously reduce the power of the current sample: the low MZ and DZ correlations for the phobia diagnoses and scales, and the ordinal level of measurement [34, 55]. In the present case, the apparent shared and random environment model of variation of blood-injury phobias might be the correct answer, but it rests on the rather flimsy evidence of a .32 DZ tetrachoric correlation. That this correlation could be half of the MZ value (.33) is not rejected by the data, so we must regard the support for the social learning model as weak.

REFERENCES


APPENDIX

To test the power of twin data to resolve fear and phobia dimensions, we simulated contingency tables using two independent normal distributions. The first distribution had a single threshold which differentiated between those who had vs. did not have fear. The second distribution had two thresholds which differentiated those with fear into three interference groups: none, minor, and major. Thresholds were selected to yield the same proportions of the four groups that we observed in our data. Power to detect deviations from bivariate normality depends on the twin correlation for the two distributions; the greater the difference between them, the greater the power. Also, larger correlations are more informative than small ones. However, the simulations showed that even if the fear dimension correlated .6 between twins and the (independent) interference dimension correlated .3, we would require 6,679 pairs of twins to have 90% power of rejecting (at the .05 level of significance) the hypothesis that a single, bivariate normal distribution was behind the observed contingency table pattern.