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Major depression and phobias: the genetic and environmental sources of comorbidity

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SYNOPSIS In a population based sample of 2163 personally interviewed female twins, substantial comorbidity was observed between DSM-III-R defined major depression (MD) and 4 subtypes of phobia: agoraphobia, social phobia, animal phobia and situational phobia. However, the level of comorbidity of MD with agoraphobia was much greater than that found with the other phobic subtypes. We conducted bivariate twin analyses to decompose the genetic and environmental sources of comorbidity between MD and the phobias. Our results suggest that a modest proportion of the genetic vulnerability to MD also influences the risk for all phobic subtypes, with the possible exception of situational phobias. Furthermore, the magnitude of comorbidity resulting from this shared genetic vulnerability is similar across the phobic subtypes. By contrast, the non-familial environmental experiences which predispose to depression substantially increase the vulnerability to agoraphobia, have a modest impact on the risk for social and situational phobias and no effect on the risk for animal phobias. The increased comorbidity between MD and agoraphobia results, nearly entirely, from individual-specific environmental risk factors for MD which also increase the risk for agoraphobia but not for other phobias.

INTRODUCTION

Major depression (MD) and phobias are among the most common of psychiatric disorders (Robins *et al.* 1984; Robins & Regier, 1991). Of the epidemiological and clinical studies that have examined these two syndromes, most (Schapira *et al.* 1970; Boyd *et al.* 1984; Koehler *et al.* 1986; Thompson *et al.* 1989; Angst *et al.* 1990), but not all (Barlow *et al.* 1986), have documented high rates of comorbidity. Furthermore, the rates of comorbidity with MD appear to differ in the phobic subtypes, being highest in agoraphobia, intermediate in social phobia, and lowest in the simple phobias (Schapira *et al.* 1970; Boyd *et al.* 1984; Angst *et al.* 1990; Sanderson *et al.* 1990).

For disorders such as MD (Tsuang & Faraone, 1990; Kendler *et al.* 1992*a*) and phobias (Rose *et al.* 1981; Rose & Ditto, 1983; Neale & Fulker, 1984; Marks, 1987; Philips *et al.* 1987; Kendler *et al.* 1992*b*), whose aetiology is influenced by familial factors, genetic epidemiological approaches can test critical hypotheses about the causes of comorbidity that cannot be addressed in epidemiological samples. In particular, the relative importance of three causes of comorbidity can be assessed. First, MD and phobias may tend to co-occur because some of the genes which influence vulnerability to depression also influence the vulnerability to phobias. Secondly, two disorders may co-occur because familial–environmental factors predispose to both disorders. For example, certain parental rearing patterns may increase the risk for the development of both depression and phobias (Parker, 1983). Thirdly, two disorders may co-occur because non-familial environmental factors may increase the risk for both disorders. For example, certain classes of stress-

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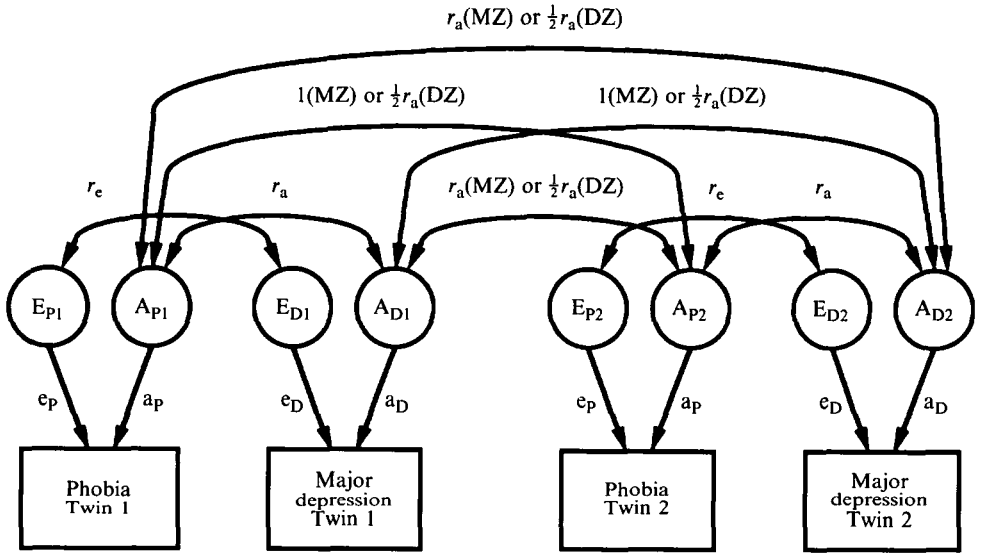


FIG. 1. A full bivariate twin model depicted for Major Depression (abbreviated as D) and Phobia (abbreviated as P) in twin 1 and twin 2 of a twin pair. Common or familial environmental effects have not been included to avoid confusing complexity. The variance in liability to each disorder is divided into that due to additive genetic effects (A_D and A_P, respectively, and individual specific environment (E_D and E_P, respectively). Paths, which equal standardized regression coefficients the values of which must be squared to equal the proportion of variance accounted for, are represented by lower case letters (a and e). The phenotypic correlation between major depression and phobia is, in this model, decomposed into that due to the correlation of additive genes (r_a), and the correlation of individual specific environmental risk factors (r_e). Thus, E_{P1} represents the individual specific environmental factors influencing phobias in twin 1 while A_{D2} is the additive genetic factors influencing major depression in twin 2.

ful events might predispose both to MD and to phobias (Brown & Harris, 1978; Marks, 1987).

The resolution of all three causes of comorbidity requires the collection of twin or adoption data. While family studies can distinguish the third from the first two causes, they cannot discriminate between genetic and familial–environmental sources of comorbidity. In this report, we attempt to clarify, in a population-based sample of female twins, the causes of the comorbidity between MD and 4 kinds of phobias: agoraphobia, social phobia, animal phobia and situational phobia.

METHOD

As outlined in detail elsewhere (Kendler *et al.* 1992*a*,*b*,*c*), as part of a longitudinal study of genetic and environmental risk factors for common psychiatric disorders in women, we personally interviewed 2163 female twins, including both members of 1033 pairs, from the population-based Virginia Twin Register, with a mean age (±S.D.) of 30·1±7·6. The refusal rate during the personal interviews phase, conducted by interviewers with Master's degrees in Social Work or Bachelor's degrees and at least two years clinical experience, was 8%. Of the completed interviews, 89% were in person and 11% by phone. All individuals were interviewed by an individual blind to the psychopathological status of their co-twin. All zygosity information from the 1033 pairs where both members were interviewed was reviewed by two experienced researchers of twins who were blind to information about the psychiatric status of the twins. Information reviewed included data on physical similarity and frequency of confusion as children (which have been shown to be capable of determining zygosity with around 95% accuracy) (Eaves *et al.* 1989) and, in over 80% of cases, photographs of both twins. On the basis of this review, twin pairs were classified into 5 groups: definitely monozygous (MZ), definitely dizygous (DZ), probably MZ, probably DZ and zygosity uncertain. We attempted to obtain blood samples from both members of all pairs in the final 3 categories and were successful in 119 out of the 186 pairs. Zygosity

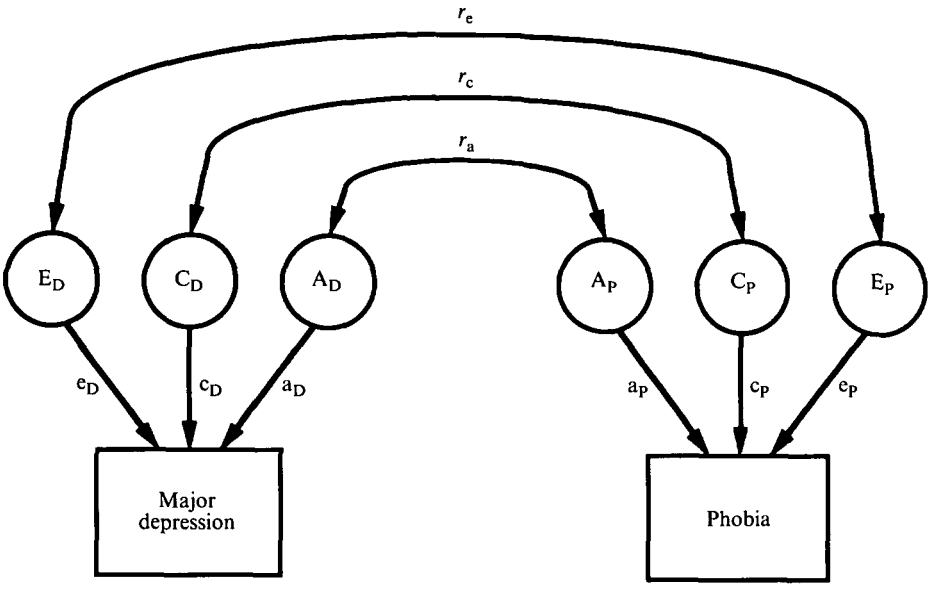


FIG. 2. A schematic full bivariate twin model for Major Depression and Phobia, which represents a simplification of the model presented in FIG. 1. It differs from this former figure in also presenting common or familial environment for major depression and phobia (C_D and C_P, respectively, with the path abbreviated as c and the correlation between them as r_c).

was determined by the examination of DNA polymorphisms, using 8 highly informative probes, which, if all identical, produced a probability of monozygosity of 0·9997 (Spence *et al.* 1988). Final zygosity determination, which used blood samples where available and otherwise a definite or probable zygosity diagnosis, yielded 590 MZ twin pairs, 440 DZ twin pairs and 3 pairs classified as of uncertain zygosity. DNA methods validated our zygosity diagnosis in 87 of 105 (83%) twin pairs in the 'probable' category and 26 of 26 pairs in the 'definite' category. The probable error rate in zygosity assignment in the total sample is almost certainly less than 2%.

Lifetime prevalence for MD was assessed using an adapted version of the Structured Clinical Interview for DSM-III-R Diagnosis (Spitzer *et al.* 1987) and the diagnosis, using DSM-III-R criteria (American Psychiatric Association, 1987), was made by K.S.K. after a blind review of the interview protocols. Phobias were assessed by an adaptation of the Phobic Disorders section of the Diagnostic Interview Schedule (DIS) Version III-A (Robins & Helzer, 1985), which in turn was based on the DSM-III criteria (American Psychiatric Association, 1980). In brief, the list of the 17 specific unreasonable fears listed in the DIS was modified, dropping some 'miscellaneous' and blood-injury fears and expanding the list of animal and situational fears. Instead of asking the respondent individually about a series of fears, the fears were grouped into 4 categories: agoraphobia – going out of the house alone, being in crowds and being in open spaces; social phobia – meeting new people, giving a speech, using public bathrooms and eating in public; animal phobias – bugs, spiders, mice, snakes and bats; situational phobias – tunnels, other closed places, bridges, airplanes and other high places. While the DIS assessed interference by asking the respondent whether the fear interfered with their 'life or activities a lot', we had interviewers assess, with additional probing if necessary, whether the irrational fear had significant behavioural impact on the respondent's life. Of the total number of 'unreasonable' fears 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 relatively persistent fear which the respondent recognizes as unreasonable and that, in the judgement of the interviewer, significantly interferes, in objective behavioural terms, in the respondent's life.

Inter-rater reliability, as measured by chance corrected agreement or κ (Cohen, 1960), was assessed on 53 jointly conducted interviews with the following results: major depression (MD), $\kappa = 0{\cdot}96 \pm 0{\cdot}04$; and phobia $\kappa = 0{\cdot}73 \pm 0{\cdot}10$; agoraphobia, $\kappa = 1{\cdot}00 \pm 0{\cdot}06$; social phobia, $\kappa = 1{\cdot}00 \pm 0{\cdot}08$; animal phobia, $\kappa = 0{\cdot}50 \pm 0{\cdot}21$; and situational phobia, $\kappa = 0{\cdot}89 \pm 0{\cdot}07$.

Statistical analysis

In standard univariate twin analysis, the goal is to decompose the variance in liability to a given disorder into genetic and environmental components. In bivariate analyses, the goal is to decompose the covariance between two disorders, such as MD and phobias into that due to genes, shared environmental and individual specific environment. A reduced version of the full bivariate model (eliminating effects of common environment) (Heath *et al.* 1989; Neale *et al.* 1989) is illustrated in Fig. 1 and a more schematic version including common environment in Fig. 2. Basically, bivariate analysis subdivides an observed or 'phenotypic' correlation of liability between two disorders into three parts that are due to: (*i*) the same additive genes predisposing to both disorders (the additive genetic correlation or r_a); (*ii*) the same shared or common familial environmental factors predisposing to both disorders (the common or shared environmental correlation or r_c); and (*iii*) the same individual-specific environmental risk factors predisposing to both disorders (the individual-specific environmental correlation or r_e). While univariate genetic analysis is conducted on the correlation of a variable in MZ and DZ twin pairs, bivariate analysis examines three kinds of correlations: within variable cross-twin, within twin cross-variable and cross-twin cross-variable.

Tetrachoric correlations were estimated by the computer program PRELIS (Jöreskog & Sörbom, 1988), assuming a liability-threshold model directly from the 2×2 tables listing the affection status of each twin. Since we are working with a general population sample, no ascertainment correction is needed. Model fitting to these correlations of liability was performed by the computer program LISREL using asymptotic weighted least squares (Heath *et al.* 1989; Jöreskog & Sörbom, 1989; Neale *et al.* 1989). The best fitting model was chosen using Akaike's information criterion (AIC) (Akaike, 1987), which is calculated as χ^2 minus twice the degrees of freedom, and reflects both the goodness of fit and parsimony of the model. The goal was to produce the model with the most *negative* value for AIC. Dominance genetic variance is not included in our analyses because previous univariate analyses of MD (Kendler *et al.* 1992*a*) and phobia (Kendler *et al.* 1992*b*) failed to demonstrate its importance for either disorder.

The comorbidity between MD and phobias that is due to genetic, common environmental and individual-specific environmental factors can be calculated from the best fitting model and equal, using the terminology depicted in Fig. 2, $a_D r_a a_P$, $c_D r_c c_P$, and $e_D r_e e_P$, respectively. In the interest of space, we present only the fit and not the estimated parameter values for all intermediate models. Full results are available on request.

RESULTS

Prevalences and odds ratios

As previously reported (Kendler *et al.* 1992*a*,*b*), the lifetime prevalence for major depression (MD) and any phobia in this sample of 2163 personally interviewed female sample is 31 and 33%, respectively. The lifetime prevalences for the four phobic subtypes are: agoraphobia, 9%; social phobia, 12%; animal phobia, 11%; and situational phobia, 12%.

Table 1 depicts the odds ratio and the tetrachoric correlation between MD, any phobia and the 4 phobia subtypes. For MD and any phobias, both the odds ratio (2·26) and the tetrachoric correlation ($+0{\cdot}30 \pm 0{\cdot}03$) indicated a significant association in this sample between the diagnosis of MD and phobia. Significant associations were also found between MD and the individual phobia subtypes. However, as measured both by the odds ratio and the tetrachoric correlation, the association of MD with agoraphobia was over twice as strong as that found with any of the other phobic subtypes.

Twin model fitting

Any phobia

In order to clarify the causes of comorbidity between MD and phobias, we proceeded to bivariate twin analysis. As outlined in Table 2,

Table 1. *Comorbidity between major depression and phobias as assessed by the odds ratio and tetrachoric correlation*

Phobia	Odds ratio		Tetrachoric correlation ±S.E.
	Estimate	95% CI	
Any	2·26	1·86–2·73	0·30±0·03
Agoraphobia	4·91	3·58–6·72	0·47±0·04
Social	2·09	1·52–2·60	0·22±0·04
Animal	1·56	1·16–2·03	0·14±0·05
Situational	2·12	1·63–2·75	0·24±0·04

CI = Confidence interval.

we began with the full model pictured in Fig. 2, which included for both any phobia and MD additive genetic, common environmental and individual specific environmental factors (A, C and E, respectively) and allowed all three sets of aetiological factors for any phobia and for MD to be correlated. That is, the comorbidity between MD and phobia could be due to genetic, familial environmental or specific environmental factors that influence the liability to both disorders. The full model (model I) fits very well ($\chi^2 = 2{\cdot}15$, df = 5, AIC = −7·85). In model II, the common environmental component for depression (C_D) was set to zero and so r_c becomes undefined. The fit of this model was identical to model I ($\chi^2 = 2{\cdot}15$), and because it contains two less parameters (df = 7), it had a much better AIC (−11·85). In model III, the common environmental component for any phobia (C_P) was also set to zero. The fit of the model still does not change ($\chi^2 = 2{\cdot}15$), but with one less parameter (df = 8), the AIC is still better (−13·85).

We then fitted 4 modifications of model III: (*i*) r_a at zero (model IV); (*ii*) r_e at zero (model V); (*iii*) r_a at one (model VI), and (*iv*) r_e at one (model VII). Models IV and V postulate that all the comorbidity between MD and any phobia results from individual specific environmental or genetic risk factors, respectively, that influence the liability to both disorders. Models VI and VII hypothesize that all the genes or all the individual specific environmental risk factors that impact on depression are equally pathogenic for any phobia. As seen in Table 1, none of these models produced an AIC that was superior to that found with model III, suggesting that the true values for r_a and r_e are greater than zero but less than one.

The parameter estimates of the best fitting submodel (model III) are shown in Fig. 3 and suggest that there is a modest correlation between the individual specific environmental

Table 2. *Results of model fitting for agoraphobia, social phobia and simple phobia*

Model	I	II	III	IV	V	VI	VII
Depression	ACE	AE	AE	AE	AE	AE	AE
Phobia	ACE	ACE	AE	AE	AE	AE	AE
r_a	F	F	F	0	F	1	F
r_c	F	—	—	—	—	—	—
r_e	F	F	F	F	0	F	1
df	5	7	8	9	9	9	9
Any phobia							
χ^2	2·2	2·2	2·2	4·7	16·2	18·6	33·3
AIC	−7·9	−11·9	−13·9*	−13·4	−1·4	+0·6	+15·3
Agoraphobia							
χ^2	6·2	6·2	6·2	12·3	23·0	14·2	14·3
AIC	−3·8	−7·8	−9·8*	−5·7	+5·0	−3·8	−3·7
Social							
χ^2	6·0	6·6	6·6	10·2	9·2	14·7	38·6
AIC	−4·0	−7·4	−9·4*	−7·8	−8·9	−3·3	+20·6
Animal							
χ^2	11·4	11·4	11·4	13·6	12·0	21·6	48·4
AIC	+1·4	−2·6	−4·6	−4·4	−6·0*	+3·6	+30·4

A, Additive genetic factors; C, common or familial environmental factors; E, individual specific environmental factors; r_a, additive genetic correlation; r_c, common environmental correlation; r_e, individual specific environmental correlation; *F*, free (parameter free to take any value); 0, 1, parameter fixed at 0 or 1; df, degrees of freedom; AIC, Akaike's Information Criterion; *, best fitting model by Akaike's Information Criterion (Akaike, 1987).

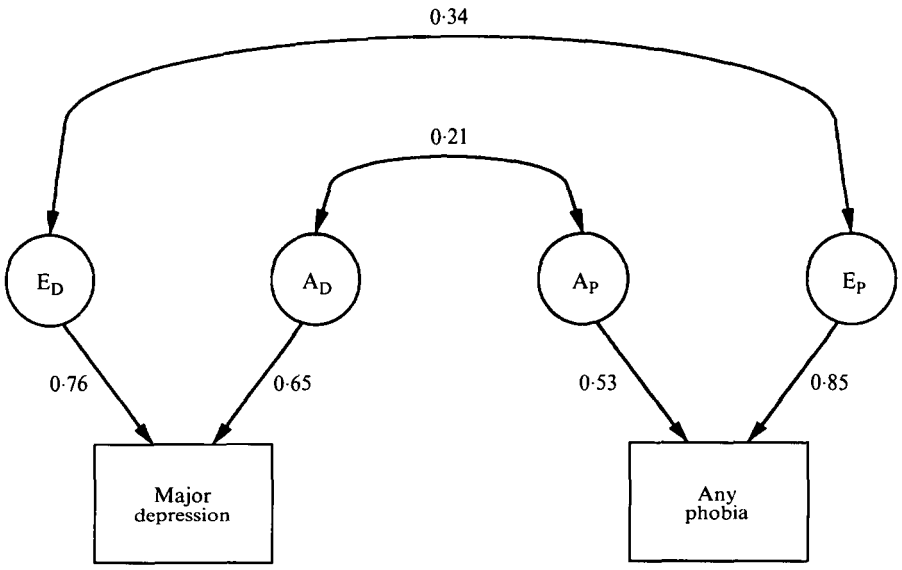


FIG. 3. The parameter estimates from the best-fitting submodel (model III in Table 2) for major depression and any phobia.

risk factors for MD and any phobia (+0·34) and a small, but significant, correlation between the additive genetic factors that influence the two syndromes (+0·21).

Agoraphobia

The basic pattern of results for MD and agoraphobia was similar to that found for MD and any phobia (Table 2). The full model (model I) fitted well ($\chi^2 = 6{\cdot}18$, df = 5, AIC = −3·82) and the fit remained the same and the AIC improved when the common environmental component for depression (model II) and then for agoraphobia (model III) were set to zero. Models IV through VII all fitted much worse than model III, indicating that the true values for r_a and r_e between agoraphobia and MD are both greater than zero but less than one.

The parameter estimates of the best fitting submodel (model III) are seen in Fig. 4*a* and suggest that there is a substantial correlation between the individual specific environmental risk factors for MD and agoraphobia (+0·53) and a more modest correlation between the additive genetic factors that influence the two disorders (+0·38).

Social phobia

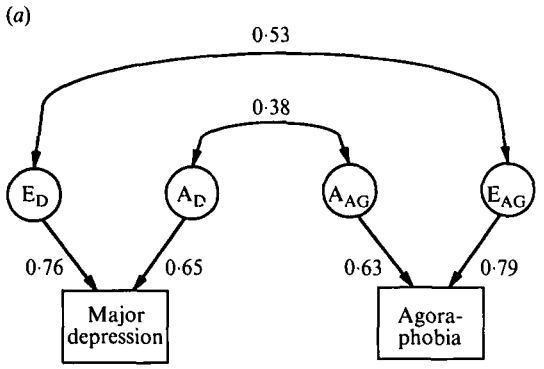
The pattern of results for social phobia were the same as those found for any phobia and agoraphobia (Table 2). Model III was again the best fitting submodel. As seen in Fig. 4*b*, however, the estimated correlation between the environmental factors which predispose to MD and social phobia was much smaller than that seen for agoraphobia and MD (+0·18), while the genetic correlation was only slightly smaller (+0·30).

Animal phobia

For animal phobia, as with the previous phobias, model III fitted better than models I or II, indicating that familial environmental factors for both depression and animal phobia could be deleted from the model with an associated improvement in the AIC (Table 2). Unlike the previous results, however, the AIC improved when r_e was set to zero (model V), leaving model V with a lower AIC value than model III. As with the other phobias, models IV, VI and VII produced poor fits. As seen in Fig. 5*a*, the best fitting model for animal phobia and depression suggests that comorbidity arises solely from a correlation in additive genetic effects of modest magnitude (+0·33).

Situational phobia

The results of model fitting for situational phobia differed substantially from those found for any of the other phobias (Table 3). Model I fit only



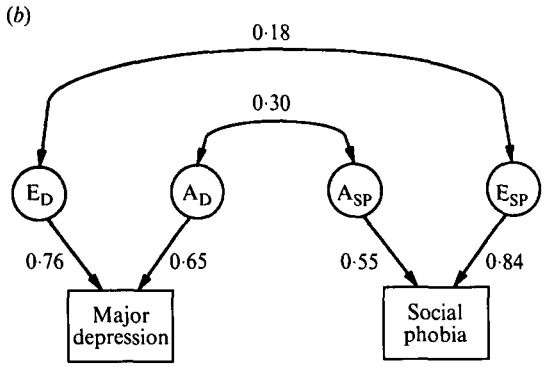
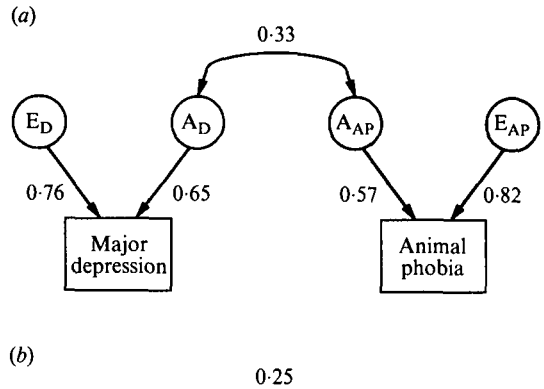


FIG. 4(*a*). The parameter estimates from the best-fitting submodel (model III in Table 2) for major depression and agoraphobia. (*b*). The parameter estimates from the best-fitting submodel (model III in Table 2) for major depression and social phobia.



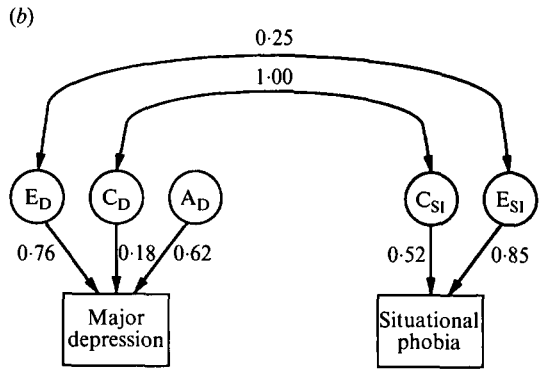


FIG. 5(*a*). The parameter estimates from the best-fitting submodel (model V in Table 2) for major depression and animal phobia. (*b*). The parameter estimates from the best-fitting submodel (model IV in Table 3) for major depression and situational phobia.

marginally ($\chi^2 = 10{\cdot}2$, df = 5, $P < 0{\cdot}10$) and this fit improved modestly and nearly equally either when the common environment in depression (model II) or the additive genes for situational phobias (model III) were set to zero. However, if model III was now modified so that r_c was set to unity (model IV), the best AIC was produced. This fit was not improved when r_e was set to unity (model V) or set to zero (model VII) or when r_c was set to zero (model VI). The parameter estimates of the best fitting model, seen in Fig. 5*b*, suggest that the comorbidity between MD and situational phobias results from a modest correlation of individual-specific

Table 3. *Results of model fitting for situational phobia*

Model	I	II	III	IV	V	VI	VII
Depression	ACE	AE	ACE	ACE	ACE	AE	AE
Phobia	ACE	ACE	CE	CE	CE	CE	CE
r_a	F	F	—	—	—	—	—
r_c	F	—	F	1	1	—	1
r_e	F	F	F	F	1	F	0
df	5	7	7	8	9	9	9
Situational phobia							
χ^2	10·2	10·5	10·3	10·3	47·4	14·9	17·2
AIC	+0·2	−3·6	−3·7	−5·7*	+29·4	−3·1	−0·8

A, Additive genetic factors, C, common or familial environmental factors; E, individual specific environmental factors; r_a, additive genetic correlation; r_c, common environmental correlation; r_e, individual specific environmental correlation; F, free (parameter free to take any value); 0, 1, parameter fixed at 0 or 1; df, degrees of freedom; AIC, Akaike's Information Criterion; *, best fitting model by Akaike's Information Criterion (Akaike, 1987).

Table 4. *The absolute correlation in liability between major depression and phobias due to shared genetic, common environmental and individual specific environmental factors based on the best-fitting model*

	Additive genetic		Common environmental		Unique environmental	
Phobia	*r*	%	*r*	%	*r*	%
Any	0·07	24	—	—	0·22	76
Agoraphobia	0·16	33	—	—	0·32	67
Social	0·11	48	—	—	0·12	52
Animal	0·12	100	—	—	—	—
Situational	—	—	0·09	36	0·16	64

environmental risk factors (+0·25) and a perfect correlation for familial environmental risk factors.

Decomposing the sources of comorbidity

Table 4 depicts, from the best-fitting models, the estimated correlations in liability between MD and phobias that are due to additive genetic, common environmental and individual-specific environmental factors. For MD and the three phobic subtypes with comparable best-fitting models (agoraphobia, social phobia and animal phobia), the correlations in liability that result from genetic factors which influence the liability to both disorders are modest and similar in magnitude (0·11 to 0·16). However, a quite different pattern is seen for the individual-specific environmental factors that influence risk to both disorders, which produce a correlation in liability between MD and agoraphobia (0·32) that is far greater than that seen between MD and any other phobic subtype.

Table 4 also shows the proportion of the observed comorbidity that is due to genetic and environmental factors. For example, about 75% of the observed comorbidity between MD and any phobia in our sample is due, according to our results, to unique environmental risk factors shared by both syndromes. Only 25% of the observed comorbidity is due to genetic factors which influence the liability to both disorders. It is interesting that unique environmental risk factors are responsible for the majority of the observed comorbidity between MD and all phobic subtypes except animal phobia.

DISCUSSION

In an epidemiological sample of female twins, significant comorbidity was found between major depression (MD), as defined by DSM-III-R (American Psychiatric Association, 1987) and any phobia and each of four subtypes of phobia, agoraphobia, social phobia, animal phobia and situational phobia. Consistent with previous studies (Schapira *et al.* 1970; Boyd *et al.* 1984; Angst *et al.* 1990; Sanderson *et al.* 1990), the magnitude of the comorbidity with MD was substantially higher for agoraphobia than for the other subtypes of phobias. We could not, however, replicate previous findings that the comorbidity between MD and social phobia was substantially greater than that found between MD and situational phobias (Schapira *et al.* 1970; Sanderson *et al.* 1990).

Using bivariate twin analysis, we sought to understand the causes of the observed comorbidity between MD and phobias. For agoraphobia, social phobia and animal phobia, although the best fitting model indicates the existence of genetic factors which predispose to both disorders, the magnitude of the correlations between the genetic factors was modest, ranging from +0·30 to +0·38.

For agoraphobia, social phobia and situational phobia, the best fitting model indicates the existence of individual specific environmental factors that predispose to these phobias and depression. Here, the range of correlations was quite wide, ranging from +0·18 (social phobia) to +0·53 (agoraphobia). By contrast, for animal phobias, the best fitting model indicated that the environmental risk factors for this disorder did not correlate with those for depression.

The results for situational phobia were anomalous. This was the only phobic subtype for which common or familial environment was found to be important. Here, the best fitting bivariate model indicated that around a third of the covariance between situational phobia and MD was due to a set of familial environmental risk factors which were pathogenic for the two disorders. Our confidence in these results is diminished for two reasons. First, while these

familial environmental factors are perfectly correlated in MD and situational phobia, they account for a trivial proportion of variance in liability to depression (approximately 3%, compared to 58 and 38%, respectively for unique environmental and genetic factors). Secondly, multivariate model-fitting with the four phobia subtypes (Kendler *et al.* 1992*b*) does not provide strong support for the hypothesis that the source of variance in liability to situational phobias is qualitatively different from that found for the other phobia subtypes.

Bivariate twin analysis allows us to decompose the observed comorbidity between MD and phobias into that due to genetic risk factors and environmental risk factors. Although genetic factors played a significant role in the aetiology of the comorbidity between MD and phobias, their role was a modest one. Furthermore, estimates of the correlations in liability that were due to these shared genetic factors were quite similar between MD and the three phobic subtypes with comparable best-fitting models (agoraphobia, social phobia and animal phobia). Our results suggest that the large differences in the magnitude of the observed comorbidity between MD and the phobic subtypes are not the result of genetic factors.

By contrast, the magnitude of the comorbidity resulting from environmental risk factors pathogenic for both MD and phobias is both larger on average, but also much more highly variable across phobic subtypes than that found for shared genetic risk factors. In particular, the correlation in liability due to environmental risk factors was at least twice as great between MD and agoraphobia as between MD and any other phobic subtypes. Our results indicate that the much greater comorbidity observed between MD and agoraphobia *v.* other phobic subtypes results nearly entirely from the much larger proportion of individual-specific environmental risk factors shared by the MD and agoraphobia.

These results also provide interesting information on the nature of the environmental risk factors for phobias. In a multivariate genetic analysis of the subtypes of phobias, we previously found that 'non-specific' environmental risk factors that were pathogenic for all phobic subtypes were most important for agoraphobia and least important for animal phobias (Kendler *et al.* 1992*b*). Our present results confirm and expand on those findings. A substantial proportion of the environmental risk factors for agoraphobia appear to be quite non-specific in that they are shared not only with other phobias but also with MD. By contrast, for animal phobias, these environmental risk factors appear to be much more specific in that they have little or no impact on the risk for other phobias or for MD.

Limitations

These results apply only to women and it is possible that the factors influencing the co-occurrence of MD and phobias might differ significantly across genders. Because MD was used in each of our bivariate analyses with a different phobic subtype, the results obtained from these analyses are not uncorrelated.

Our bivariate model assumed that the comorbidity between phobias and MD resulted from shared risk factors, rather than the liability of one disorder directly influencing the liability to the other. While such a 'causal' model can be tested in the twin design (Neale & Cardon, 1992), power to discriminate between alternative models in cross-sectional data would be very low when working with dichotomous variables which have similar and modest levels of heritability.

The lifetime prevalence rates for MD and phobias in this sample are relatively high. This is probably due to several factors. First, both conditions are broadly defined in this study. 'Major' depression in DSM-III-R (American Psychiatric Association, 1987) might not be considered 'major' by European clinical standards, requiring only 5 of 9 symptoms for a minimum of two weeks and neither impairment nor help-seeking. Of those diagnosed with MD in this sample, only 31% reported extensive impairment associated with their worst episode and only 38% ever sought professional help for their depression. While phobias are also broadly defined in this sample and do not require help-seeking for the diagnosis, this definition does differ critically from 'phobic fears' assessed by self-report questionnaire (e.g. Torgersen, 1979; Philips *et al.* 1987). The diagnosis of phobia in this report was given only when a relatively persistent unreasonable fear was accompanied

by behavioural impairment judged significant by the clinically trained interviewer.

Secondly, the epidemiological sample studied in this report was younger than most previous population samples. The apparent cohort effect for MD (Klerman *et al.* 1985) may therefore also be partly responsible for the high observed prevalence rates in this sample.

Thirdly, rates of MD and phobias in this study were also higher than in several recent epidemiological studies in women that used similar diagnostic criteria (Robins *et al.* 1984; Canino *et al.* 1987; Wells *et al.* 1989; Weissman *et al.* 1991). However, these studies all employed lay-interviewers and a highly structured psychiatric interview, the DIS (Robins & Helzer, 1985), a procedure which may underestimate the population rates of major psychopathology (Parker, 1987). Prior to our probe questions for lifetime psychiatric disorders, we emphasized the need for the respondent to take time to think back over her entire life before answering. This probably increased our ascertainment rate for prior episodes of major depression because our ratio of lifetime to one-year prevalence (3·3:1) is much higher than that obtained in women in the Epidemiologic Catchment Area Study (1·75:1) (Weissman *et al.* 1991). Furthermore, several recent population-based studies, including at least one with very similar methods (Weissman & Myers, 1978), report lifetime prevalence rates for broadly defined depression in women that are similar to or higher than those reported here (Bebbington *et al.* 1989; Rorsman *et al.* 1990). Our interviewer-based assessment of impairment in phobias, while more objective, may produce a lower 'threshold' for interference than the self-report measure used in the DIS. However, the lifetime prevalence rates of phobia were quite variable in the four ECA sites with comparable information (Eaton *et al.* 1991). The rates found for any phobia in Caucasian females in Baltimore and the Piedmont (25·0 and 22·8%, respectively, W. Eaton PhD, personal 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.

Finally, since we examined these twins at only one time point, we were unable, in these analyses, to incorporate unreliability of assessment into our models. In fitting bivariate models, unreliability of measurement might have a substantial impact if a 'self-report bias' is substantially correlated for disorders assessed in an individual at the same interview (e.g. MD and phobia), but not highly correlated in twin pairs. For example, if as a result of interviewer–respondent interactions, some respondents felt quite willing and others were quite hesitant to admit to any psychopathology, this would lead to an overestimation of the individual specific environmental correlation between the two disorders.

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