A Twin-Family Study of Self-Report Symptoms of Panic-Phobia and Somatization

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Self-report symptoms of anxiety are widely used in mental health and social science research as an index of current psychiatric state. Previous twin studies have suggested that genetic factors account for a significant proportion of the variance in these symptoms. To replicate and extend these findings, we examined self-report symptoms of panic–phobia and somatization in the "Virginia 30,000" twin-family sample. Model fitting applied to 80 unique relationships in the twin-family pedigree produced the following major results: (i) genetic effects were significant for both symptom factors, accounting for between 25 and 49% of the total variance, with the exception of symptoms of panic–phobia in females, where they accounted for 15–16% of the variance; (ii) familial environmental effects were absent for symptoms of somatization, while for symptoms of panic–phobia they accounted for a very small proportion of variance in males ($\leq 1.2\%$) and a modest proportion in females (6–17%); (iii) spousal correlations were present for both factors, ranging from +0.05 to +0.20; (iv) genetic factors which influenced symptoms were generally the same in males and females, although their effect was greater in males; (v) heritability estimates were lower in the population-based than in the volunteer sample; and (vi) when test–retest reliability was included in the model, results suggest that genetic factors account for at least half of the stable variance for all symptom factors, except panic–phobia in females. Our results support the validity of previous twin studies of self-report symptoms of anxiety and suggest that genetic factors significantly influence these symptoms but familial-environmental factors play little or no etiologic role.

INTRODUCTION

Symptoms of anxiety as assessed by self-report are widely used by the psychiatric and social sciences

in clinical and epidemiologic research (Turner and Noh, 1983; Andrews *et al.*, 1978; Williams *et al.*, 1981; Vingerhoets and Van Heck, 1990; Goldberg *et al.*, 1987). The major value of such scales is that they provide a convenient and broadly valid measure of current psychiatric symptomatology or, seen from another perspective, psychological well-being.

Self-report symptom scales were initially conceptualized as "state" measures. However, it is now clear that such symptoms have considerable temporal stability and reflect, at least in part, stable or "trait"-like aspects of psychiatric functioning (Duncan-Jones *et al.*, 1990).

In both clinical and general population sam-

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ples, high variability is consistently shown in self-report measures of anxiety (Turner and Noh, 1983; Andrews *et al.*, 1978; Williams *et al.*, 1981; Goldberg *et al.*, 1987). Several studies from large twin populations have suggested that a considerable proportion of variance in these symptoms results from genetic factors (MacKinnon *et al.*, 1990; Martin *et al.*, 1988; Jardine *et al.*, 1984). In contrast, these same studies suggest that family environment has little or no impact on symptoms of anxiety.

In this report, we attempt to extend and replicate these previous findings by examining self-report symptoms of anxiety in twins and their families. The twin-family design has important advantages over the use of twins alone (Heath *et al.*, 1985). First, it permits an evaluation of the validity of key assumptions of the twin model. Can the results obtained in twins be extrapolated to those found in other, more common relationships? Second, twin studies are intragenerational. Twin family studies can address central questions about the causes of familial transmission from parents to their offspring. Third, the twin-family design permits a much finer discrimination of environmental causes of familial resemblance. While twin studies are restricted to a single category of "common" or "familial" environment, twin-family studies can discriminate three major forms of familial environment: vertical cultural transmission (VCT), in which behavior in parents leads directly to similar behavior in their offspring, sibling environment (other environmental factors unrelated to parental behavior which make siblings reared in the same household similar), and twin environment (environmental factors that make twins more similar than nontwin siblings).

METHODS

Sample

As outlined in detail elsewhere (Truett *et al.*, 1994; Kendler *et al.*, 1994), data for this study were obtained from two sources: a volunteer twin sample solicited through an American Association of Retired Persons (AARP) newsletter and the Virginia Twin Registry. The Virginia Twin Registry is a population-based register, constructed from a systematic review of public birth records in the Commonwealth of Virginia. Current addresses are obtained by matching these records with other pub-

lic records and from other relatives. Twins obtained through either source were asked to provide names and addresses of spouses and first-degree relatives. An ideal pedigree will thus contain a pair of twins and their spouses, parents, siblings, and offspring. Inclusion in the study was based only on an individual's willingness to return a mailed questionnaire covering health and lifestyle issues. The sample had a lower age limit of 18 years and no upper age limit. Second and third mailings were sent to nonrespondents who had not indicated their refusal to participate. A telephone follow-up was conducted in an attempt to obtain complete information on pairs of twins where only one twin had responded. Completed questionnaires were received from 69.8% of the twins and 44.7% of the known relatives of these twins.

Twin zygosity is determined by responses to two questions pertaining to how often the twins were confused as children and their physical similarity. As validated against blood typing, this method has been shown to be about 95% accurate (Eaves *et al.*, 1989). For a subsample of the female Virginia twins, additional zygosity information was also available in the form of blood typing and current photographs of both twins.

A self-report symptom inventory was obtained for each participant using a 30-item subset of the 90-item Symptom Checklist (SCL-90) (Derogatis *et al.*, 1973) included in the questionnaire. Twenty-seven of these items were chosen empirically from four SCL subscales: depression (10 items), somatization (5 items), anxiety (7 items), and phobic anxiety (5 items). Three items, all dealing with sleep difficulty, were chosen from the additional items available in the SCL-90 but, aside from being included in the factor analyses, are not reported on further here.

The instructions to the individuals regarding these items were as follows:

> Below is a list of problems and complaints which people sometimes have. Read each one carefully, and circle the number (1 to 5) which best describes HOW MUCH DISCOMFORT THAT PROBLEM HAS CAUSED YOU DURING THE PAST 30 DAYS, INCLUDING TODAY.

The five possible responses were not at all, a little bit, moderately, quite a bit, and extremely.

Indices of "childhood similarity" and "current frequency of contact" were obtained from the twins. All twins were asked how often they shared

the same room, had the same playmates, were dressed alike, and were in the same classes at school (Loehlin and Nichols, 1976). They were also asked how often they were currently in contact with their cotwins, including written and telephone communication (Kendler et al., 1986). Answers to these two sets of questions were summed to form the two indices reflecting the similarity of childhood environment and current adult environment.

As part of ongoing longitudinal studies, a large number of twins from both the AARP (n = 3965) and the Virginia (n = 1433) samples completed the 30-item SCL at two points in time separated by, respectively, 14.6 ± 3.6 and 14.3 ± 3.0 months. The AARP test–retest sample contained both genders, while the Virginia sample was solely female.

Statistical Analysis

A test of the equal-environment assumption [that monozygotic (MZ) twins are no more highly correlated than dizygotic (DZ) twins for trait-relevant environmental variables] was performed using a regression analysis with the absolute difference in factor score for each twin pair as the dependent variable. We controlled for the effects of age, sex, and zygosity in these analyses, which were restricted to same-sex twin pairs.

Readers interested in the full details of the statistical analyses performed in this paper should consult Truett et al. (1994). We provide an abbreviated summary here. A factor analysis employing an oblique rotation was performed using the Statistical Analysis System (SAS Institute, 1985) with the PROMAX criteria for factor rotation on the 30 SCL items. An oblique rotation was used to facilitate interpretation of the factors with the number of factors chosen by the scree test. Each of these factor scores was corrected by multiple regression for linear and quadratic effects of age, the effects of sex and twin status, and their interactions with each other and with age. Correlations were then computed for the 80 unique one- and two-generation familial relationships present in the ideal pedigree structure using information from all families where twin zygosity was established. Multiple estimates for the same correlation (e.g., for father–son correlation, this would include father with first twin, father with second twin, father with brother of twin, etc.) were obtained separately and then

pooled into a single joint estimate (Snedecor and Cochran, 1980). Pooling correlations that are not statistically independent results in an estimate that is unbiased but with an underestimated standard error (McGue et al., 1984). McGue et al. (1984) have examined this problem in the path analysis of family data and concluded that it rarely leads to substantial biases in the estimated parameters.

This set of 80 correlations was then supplied to a specially developed model-fitting program written by L.J.E. (Truett et al., 1994). This program allows two broad classes of models to be fit to the data: sex-dependent models, which allow for sex differences in genetic and environmental factors; and sex-independent models, which do not allow for such differences. A simplified version of the full sex-independent model is shown in Fig. 1 [for a figure of the complete sex-dependent model, see Truett et al. (1994)].

Total genetic variance is divided into additive and dominance genetic effects. As outlined by Eaves (1977), we examine two different kinds of sex-dependent genetic and environmental effects. In the scalar sex-dependent model, the same genetic or environmental risk factors are acting in both genders, but the magnitude of their impact is sex dependent. In contrast, in a nonscalar sex-dependent model, different genetic and environmental factors are operating in the two genders.

The model includes the effects of nonrandom or assortative mating and assumes that spousal resemblance results from spouses selecting individuals who are similar to themselves for the relevant trait ("phenotypic" assortative mating). Vertical cultural transmission (VCT) refers to nongenetic parent–offspring transmission, where children learn or "model" their behavior from their parents. Here, VCT is modeled as a path from the phenotype of the parent to the individual-specific environment of the offspring. Four parameters are required to model VCT since mothers and fathers may affect their offspring by differing amounts and a parent may have a different impact on daughters than on sons. When both genetic and VCT transmission is present, genotype–environment correlation will arise because parents will tend to have both genotypes and phenotypes that differ from the mean in the same direction.

In addition to VCT, the model contains two other environmental sources of familial resemblance: sibling environment (other environmental
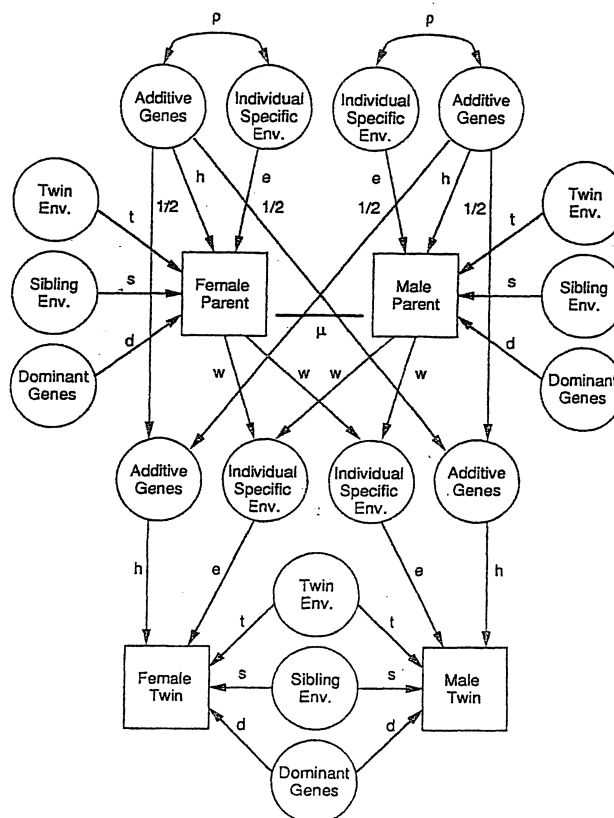
Fig. 1. A simplified model of the sources of familial resemblance depicted in a pair of opposite-sex dizygotic twins and their parents. The complete model is available on request. To avoid confusing complexity, this figure does not depict possible differences in the magnitude of individual genetic or environmental paths as a function of gender (i.e., scalar sex-dependent effects) or differences in the actual genetic or environmental factors that influence males versus females (i.e., nonscalar sex-dependent effects). The vertical cultural transmission path (w) can differ as a function of both the gender of the offspring and the gender of the parent. The model also does not depict the fact that the correlation of dominant genes in DZ twins is 1/4. The paths can be divided into the following categories. (i) *Genetic:* h--additive genes and d--dominance genes. (ii) *Familial-environmental:* w--vertical cultural transmission, s--sibling environment, and t--special twin environment. (iii) *Nonfamilial environmental:* e--unique or individual specific environment. (iv) *Assortative mating:* the copath μ. (v) *Genotype–environment correlation:* the path ρ. These paths are standardized regression coefficients, so that the total proportion of variance in the dependent variable accounted for by the individual paths equals the *square* of the path coefficient. Env., environment. Dominance genes and twin and sibling environment influence variation in all relatives but are correlated only in twins and/or nontwin siblings.

factors unrelated to parental behavior that make siblings reared in the same household similar) and twin environment (environmental factors that make twins more similar than nontwin siblings). The sibling environment is assumed to be perfectly correlated in sibling pairs (including twins) and uncorrelated in all other relatives. The twin environment is assumed to be perfectly correlated in MZ and DZ twin pairs and uncorrelated in all other relationships. The final parameter of the model

specifies the unique (or individual-specific) environment effects that are unshared with other relatives including cotwins.

Eighty unique correlations are present in these data. Our parameterization of the most general or full sex-dependent model requires the estimation of 17 parameters, thereby resulting in 63 df. All other models presented are submodels of this with parameters dropped or constrained and so have between 64 and 80 df. The estimate parameters of the full

model are additive genes (3), dominant genes (3), twin environment (3), vertical cultural transmission (4), and assortative mating (1).

The full model (Truett et al., 1994) permits the correction of results for "error" or short-term fluctuation in scale scores. We performed all standard model fitting without our data on test–retest reliability (i.e., assuming no short-term error) so that our main results would represent the sources of variance for the cross-sectional usage of the SCL. This is the way this and similar scales are most commonly used in mental health research. It should be noted, however, that in such a model, individual specific environment and error or short-term score fluctuations are confounded. Therefore, for the best-fit model for each symptom factor in our two samples, we also fit a model including reliability estimates for our data. In so doing, we describe the sources of variance for that component of SCL scores which is *stable* over time. Our ability to do this precisely in the Virginia sample was limited, since test–retest data were available only for females. Therefore, we had to assume that the stability of the SCL was equal across genders, an assumption that is not supported from the AARP data.

Model Fitting

All models were fit to the z-transformed observed correlations by iterative diagonal weighted least squares using the constrained nonlinear NAG optimizing routine E04UCF [Numerical Algorithms Group (NAG), 1978]. We tested whether the AARP and Virginia samples could be pooled into one data set by fitting the full sex-dependent model separately to the AARP and Virginia samples and then to the combined sample. The chi-square of the combined model minus the sum of the chi-squares of the individual models is a test of homogeneity with degrees of freedom equal to the combined degrees of freedom minus the sum of the individual degrees of freedom.

In most previous reports of our personally interviewed sample of twins (Kendler et al., 1992a,b), we utilized Akaike's (1987) information criterion (AIC) as an index of goodness of fit. In this report, because we are dealing with much larger sample sizes, we chose, a priori, to use the more rigorous chi-square difference test to avoid

the inclusion of parameters which explained extremely small proportions of the overall variance and yet substantially complicated the final best-fit model.

We began by fitting a full sex-dependent model and a full sex-independent model to the data. The comparison of these models determined the necessity of including sex-dependent parameters in further model fitting. Next we tested, as a group, all genetic and all environmental sources of familial resemblance. If one of these groups was not, as a whole, significant, the relevant parameters were set to zero for the remainder of the analyses. If they were significant, a set of independent tests was carried out to determine the significance of individual parameters or, in some cases, groups of parameters by independently dropping each from the model. These tests included the parameters pertaining to assortative mating, twin environment, sibling environment, vertical cultural transmission, all genes, and dominant genes. However, in the presence of significant genetic effects, we never specifically tested for the presence of additive genetic effects because a model with only dominance and no additive genetic effects is biologically unrealistic (Mather and Jinks, 1982). In the case of the sex-dependent model, sex-dependent genes were tested. Following these tests, an intermediate model was formed that contained only the parameters found to be significant. For the sex-dependent model, a second set of independent tests was performed. These tests checked whether VCT, twin environment, sibling environment, and dominant genes were sex independent. If any proved to be sex independent, a test was carried out to determine if the magnitude of their effects was sex independent. From this, a second intermediate model was formed. Upon inspection of this model, additional tests were performed as indicated by the parameter estimates and a final model was obtained.

Although relatively large, because of the modest magnitude of the observed correlations, the Virginia sample was not, by itself, able to produce an unambiguous best-fit model for the phobic anxiety and somatization symptom factors. Therefore, we proceeded with model fitting in the more numerous and more powerful AARP data and then attempted to replicate the results by applying the best-fit model obtained in the AARP sample to the Virginia sample.

Table I. Sample Size, Age, and Educational Status of Unique Individuals from the AARP and Virginia Samples[a]

| | AARP sample | | | | | Virginia sample | | | | |
| | | | | Years of education | | | | | Years of education | |
	N	Age	± SD	<HSD	≥CD	N	Age	± SD	<HSD	≥CD
MZM	1007	58.79	15.23	6.8	44.4	618	34.19	11.00	11.5	38.9
MZF	2983	60.10	14.52	8.6	24.0	1211	29.42	8.38	6.0	27.7
DZM	497	59.97	16.95	7.4	40.7	721	37.12	12.66	10.3	36.8
DZF	1726	61.82	13.74	11.0	21.8	988	30.83	8.64	7.4	25.6
DZO	1485	60.12	14.21	9.2	31.3	1307	35.77	11.95	12.0	35.2
Mothers	225	71.08	12.88	12.4	21.2	1223	57.81	9.89	17.0	26.2
Fathers	110	69.29	11.35	6.5	40.2	803	60.27	9.75	20.8	23.8
Wives	1103	61.86	8.59	7.6	27.2	773	38.00	11.41	12.2	37.3
Husbands	1904	65.00	7.40	9.3	37.1	611	37.16	10.20	12.3	37.9
Sisters	969	58.67	14.71	7.1	31.4	956	35.91	10.42	10.8	41.9
Brothers	613	58.24	15.13	6.9	46.4	648	36.11	10.04	12.9	41.0
Daughters	2893	35.52	9.15	2.2	48.7	—	—	—	—	—
Sons	1882	35.54	8.75	2.2	61.8	—	—	—	—	—
Unk zyg, ♀	1174	62.18	17.03	11.7	21.4	710	35.62	13.03	5.4	42.2
Unk zyg, ♂	561	62.37	16.12	11.7	34.1	522	40.07	13.33	13.6	24.3
Misc.[b]	71	53.77	17.03	8.6	30.0	151	45.65	16.95	20.5	24.1

[a] <HSD indicates less than high-school diploma; ≥CD, graduated from college; MZM, monozygotic male–male twin pairs; MZF, monozygotic female–female twin pairs; DZM, dizygotic male–male twin pairs; DZF, dizygotic female–female twin pairs; DZO, dizygotic opposite-sex twin pairs; unk zyg, ♀, female twins of unknown zygosity; unk zyg, ♂, male twins of unknown zygosity; misc., miscellaneous.

[b] Contains other relationships with small numbers of respondents (half-sibs, adoptive parents).

Table II. Correlations in the Panic–Phobia and Somatization Factors in the AARP and Virginia Samples for Nine Key Pooled Relationships[a]

| Relationship | Pairs (N) | AARP | | Pairs (N) | Virginia | |
		PP	Som		PP	Som
MZ twins	1,902	+0.36	+0.40	786	+0.22	+0.25
DZ twins	1,732	+0.12	+0.17	1,385	+0.11	+0.16
Parent/offspring	10,367	+0.08	+0.09	5,185	+0.02	+0.07
Full siblings	6,104	+0.06	+0.13	3,618	+0.05	+0.08
Avuncular	3,871	+0.04	+0.05	—	—	—
MZ half-siblings	1,213	−0.01	−0.05	—	—	—
Cousins	709	+0.05	+0.09	—	—	—
In-laws	6,498	+0.01	+0.02	3,265	+0.07	+0.05
Spouses	2,968	+0.07	+0.09	2,020	+0.14	+0.18

[a] AARP, American Association of Retired Persons twin sample; VA, Virginia Twin Registry sample; PP, symptoms of panic–phobia; Som, symptoms of somatization; avuncular, aunt/uncle/niece/nephew; MZ half-siblings, the offspring of one member of an MZ pair and the offspring of the other member of that pair.

The total proportion of variance due to additive and dominance genetic effects is sometimes referred to as "broad" heritability, which, for the sake of convenience, is termed here simply *heritability*.

RESULTS

Sample

The number and demographic characteristics of individuals in the AARP and Virginia samples used in this report are given in Table I. For these psychiatric symptom factors, data were available for 19,203 individuals from the AARP and 11,242 individuals from the Virginia sample. The Virginia sample contained such a small number of offspring more than 18 years of age, that this class of relatives was excluded from further analyses. Both the AARP and the Virginia samples are overwhelmingly Caucasian (99.8 and 99.9%, respectively) and have a preponderance of females (61.4 and 58.9%, respectively).

Except for factor analysis, our analyses are restricted to twin families for whom the twins' zygosity is known. The number of pairs of nine key relationships in these families is given in Table II.

Factor Analysis

Oblique factor analysis of the SCL responses from the entire AARP sample identified four read-

ily interpretable factors (Table III). The first is clearly a depression factor, the results of which have been presented elsewhere (Kendler *et al.*, 1994). The second factor contains items reflecting panic-like symptoms (terror spells, suddenly scared) and phobic behavior (avoiding frightening things, feeling afraid in open spaces or on buses or trains). Of the eight items that loaded most highly on this factor, five derived from the SCL phobic-anxiety subscale and three from the anxiety subscale. We term this a panic–phobia factor.

The third factor contains items that reflect exclusively somatic symptoms including feeling weak and faint, pains in the back and heart, and trouble getting one's breath. Of the seven items loading most heavily on this factor, five derive from the SCL somatization subscale and one each from depression (low in energy) and anxiety (heart pounding). We term this factor somatization.

The fourth factor, which we do not examine further here, was dominated by the three items that reflect sleep difficulty.

The factor analyses were repeated in the Virginia sample, with very similar results. Congruency coefficients (Derogatis *et al.*, 1972) between the factors derived from the two samples were quite high and equaled +0.991 and 0.979 for the panic–phobia and somatization factors, respectively. The factor structure was also very similar in males and females and in twin1 and twin2 from complete twin pairs.

Correlations in Relatives

Table II also presents the correlations for the panic–phobia and somatization factors in the AARP and Virginia samples for nine key relationships, pooled across genders: MZ twins, DZ twins, parent–offspring, nontwin full siblings, avuncular (uncle/aunt–niece/nephew), half-siblings (offspring of MZ twin pairs), cousins (offspring of DZ twin pairs), all in-law relationships, and spouses. Individual correlations for the 80 unique relationships are available on request.

The following seven patterns in these correlations are noteworthy. First, the correlations are all relatively modest, with none exceeding +0.40, and many below +0.10. Second, for both factors in both samples, the highest correlations were in MZ twins, which were substantially greater than those found in DZ twins. Third, for both factors in both

samples, the correlation in full siblings was less than that found in DZ twins. Fourth, the parent–offspring correlations were generally similar in magnitude to, or only slightly lower than, those found between full siblings. Fifth, with the exception of the cousins in the AARP sample (which produced anomalously high correlations), correlations in more distant relatives were generally quite low. Sixth, while most of the correlations in the different classes of relatives in the AARP and Virginia samples were broadly similar, MZ twins in the AARP sample had consistently higher correlations than MZ twins in the Virginia sample, while the opposite pattern was found for spouses. Finally, while the correlations between in-laws were generally quite low, the correlation between spouses was similar to that found in full siblings and/or DZ twins.

Before proceeding to model fitting, we tested for mean differences in the panic–phobia and somatization factor scores between 10 classes of relatives from the AARP and VA samples: mothers and fathers and male and female MZ twins, DZ twins, siblings, and spouses. Of the 20 comparisons, only 2 were significant at $p < .05$, a result which does not differ from chance expectation (Feild and Armenakis, 1974).

Model Fitting Jointly to AARP and Virginia Samples

We began by comparing the fit of the full model applied jointly to both the AARP and the Virginia samples vs. applied separately to each sample. The joint model could be strongly rejected for both the panic–anxiety (χ^2 test of homogeneity $= 54.68$, df $= 19, p = .000$) and the somatization ($\chi^2 = 49.71$, df $= 19, p = .000$) factors. Therefore, we analyzed all factors separately in the two samples.

Testing of the Equal-Environment Assumption

Prior to formal model fitting, we examined the validity of the assumption that members of MZ and DZ twin pairs were equally correlated in their exposure to environmental factors that influenced psychiatric symptoms. Controlling for zygosity, age and gender composition, we performed eight separate tests of whether the similarity of the two symptom factor scores in twin pairs, separately in the AARP

Table III. Factor Analysis of Symptom Checklist Items from the Entire AARP Sample
(n=19,203)[a]

| | Factor loading (×100) | | | |
Item summary	Factor 1. Depression	Factor 2. Panic–phobia	Factor 3. Somatization	Factor 4. Insomnia
Feeling blue	<u>80</u>	−6	0	4
Feeling worthless	<u>71</u>	8	−1	−7
Worrying too much	<u>67</u>	0	−5	15
Feeling trapped	<u>67</u>	4	−3	−6
Blaming self	<u>67</u>	5	−9	2
Feeling hopeless	<u>66</u>	11	−1	−4
No interest	<u>61</u>	−1	10	−5
Feeling tense	<u>53</u>	4	7	19
All is effort	<u>52</u>	3	29	−5
Nervous inside	<u>37</u>	15	13	12
Restless	<u>25</u>	22	3	15
Terror spells	7	<u>69</u>	2	−2
Suddenly scared	17	<u>61</u>	−6	0
Avoiding frightening things	5	<u>59</u>	4	−1
Nervous if alone	10	<u>58</u>	−1	0
Afraid of open space	−7	<u>57</u>	6	−2
Feeling fearful	37	<u>49</u>	−6	2
Afraid to travel	−11	<u>46</u>	12	1
Feeling uneasy	15	<u>39</u>	11	2
Feeling weak	17	−1	<u>60</u>	2
Heart pains	−9	8	<u>54</u>	1
Trouble getting breath	−12	18	<u>54</u>	0
Faintness	1	14	<u>46</u>	−3
Low energy	43	−16	<u>45</u>	0
Heart pounding	1	26	<u>38</u>	8
Lower back pain	13	−9	<u>31</u>	11
Loss of interest in sex	22	−6	21	4
Restless sleep	0	−3	−1	<u>92</u>
Trouble falling asleep	0	4	7	<u>62</u>
Awaking early	5	2	3	<u>57</u>

[a] Promax rotation (SAS Institute, 1985). Items that have their highest loading on that given factor and are ≥30 are underlined. The relevant interfactor correlations were as follows: factor 1–factor 2, +0.59; factor 1–factor 3, +0.52; and factor 2–factor 3, +0.46.

and Virginia samples, could be predicted by the similarity of either their childhood or their adult environments. None of these tests was significant.

Model Fitting in the AARP Sample— Symptoms of Panic–Phobia

We describe in detail model fitting for the panic–phobia factor in the AARP sample. We began with a full sex-dependent model (I; Table IV) which fit the data marginally ($\chi^2 = 89.44$, df = 63, $p < .02$). Compared with this model, a sex-independent model (II) could be rejected ($\chi^2 = 36.8$, df = 11, $p < .001$), as well as sex-dependent models without assortative mating (III) ($\chi^2 = 19.1$, df

= 1, $p < .001$), familial-environmental effects (IV) ($\chi^2 = 36.3$, df = 10, $p < .001$), or genetic effects (V) ($\chi^2 = 42.66$, df = 6, $p < .001$). We then tested specific sources of familial-environmental effects and found that we could reject a model that did not contain a special twin environment (VI) ($\chi^2 = 15.42$, df = 3, $p < .005$) or VCT (VIII) ($\chi^2 = 22.0$, df = 4, $p < .001$) but could not reject a model that lacked a special sibling environment (VII) ($\chi^2 = 0$, df = 3, NS). Testing for the specific sources of genetic resemblance, we found that we could reject a model that lacked dominance genetic effects (IX) ($\chi^2 = 28.04$, df = 3, $p < .001$), but we could not reject a model that lacked nonscalar sex-dependent additive genetic effects (X) ($\chi^2 = 0$, df = 1, NS).

Table IV. Model Fitting for Self-Report Symptoms of Panic–Phobia in the AARP Sample

Model	χ^2	df	Tested against model	Accepted/ rejected	Description
I	89.44	63	—	—	Full sex dependent
II	126.24	74	I	R	Full sex independent
III	108.58	64	I	R	No assortative mating
IV	125.70	73	I	R	No familial-environmental effects
V	132.10	69	I	R	No genetic effects
VI	104.86	66	I	R	No special twin environment
VII	89.44	66	I	A	No sibling environment
VIII	111.44	67	I	R	No vertical cultural transmission (VCT)
IX	117.48	66	I	R	No dominance genetic effects
X	89.44	64	I	A	No nonscalar sex-dependent additive genetic effects
XI	89.44	67	—	—	No sibling environment, no nonscalar sex-dependent additive genetic effects
XII	103.87	70	XI	R	No sex-dependent VCT
XIII	89.44	68	XI	A	No nonscalar sex-dependent special twin environment
XIV	100.98	69	XIII	R	No scalar sex-dependent special twin environment
XV	89.49	68	XI	A	No nonscalar sex-dependent dominance genetic effects
XVI	99.60	69	XV	R	No scalar sex-dependent dominance genetic effects
XVII	89.49	69	—	—	Model XI + no nonscalar sex-dependent special twin environment or dominance genetic effects
XVIII	89.51	70	XVII	A	No special twin environment in males
XIX	95.08	71	XVII	A	No paternal VCT
XX[a]	95.14	72	XVII	A	Model XVII + no special twin environment in males and no paternal VCT

[a] Best-fit model, which includes (i) scalar sex-dependent additive genetic, dominance genetic, and individual-specific environmental factors; (ii) maternal VCT; (iii) a special twin environment only for females; and (iv) assortative mating.

The initial stage of model fitting then was summarized in model XI, which fit exactly the same as model I but lacked both sibling environment and nonscalar sex-dependent additive genetic effects. Compared to model XI, we then found that we could reject a model that lacked sex-dependent VCT (XII) ($\chi^2 = 14.43$, df $= 3$, $p < .005$) but could not reject a model without nonscalar sex-dependent special twin environment (XIII) ($\chi^2 = 0$, df $= 1$, NS). Testing against model XIII, however, we could reject a model that lacked scalar sex-dependent special twin environment (XIV) ($\chi^2 = 11.54$, df $= 1$, $p < .001$). Again testing against model XI, we could not reject a model that lacked nonscalar sex-dependent dominance genetic effects (XV) ($\chi^2 = 0.05$, df $= 1$, NS), but (tested against model XV) we could reject a model (XVI) which did not contain scalar sex-dependent dominance genetic effects ($\chi^2 = 10.11$, df $= 1$, $p < .001$).

Model XVII summarized the next phase of our model fitting, subtracting from model XI nonscalar sex-dependent special twin environment and dominance genetic effects, with virtually no change in fit. Finally, we tested against model XVII two further simplifications and found that both could be

accepted: (XVIII) no special twin environment in males ($\chi^2 = 0.02$, df $= 1$, NS) and (XIX) no paternal VCT ($\chi^2 = 5.59$, df $= 2$, NS).

The parameter estimates of the best-fitting model (model XX; $\chi^2 = 95.14$, df $= 72$, $p = .035$) for panic–phobia in the AARP sample are shown in Fig. 2, and the proportions of variance due to specific genetic and environmental effects are summarized in Table V. The model is a relatively complex one, requiring (i) scalar sex-dependent additive genetic factors, dominance genetic factors, and individual-specific environmental factors (i.e., same genetic or environmental factors acting in males and females but differing in the magnitude of their effect), (ii) maternal VCT of greater importance for sons than for daughters, (iii) a special twin environment only for females, and (iv) assortative mating. The best-fit model predicted a substantially higher heritability in males (37.8%) than in females (16.1%). In females, special twin environment accounted for 16.2% of the variance. VCT from mothers to sons accounted for 1.2% of the variance in males and VCT from mothers to daughters accounted for 0.3% of the variance in females.
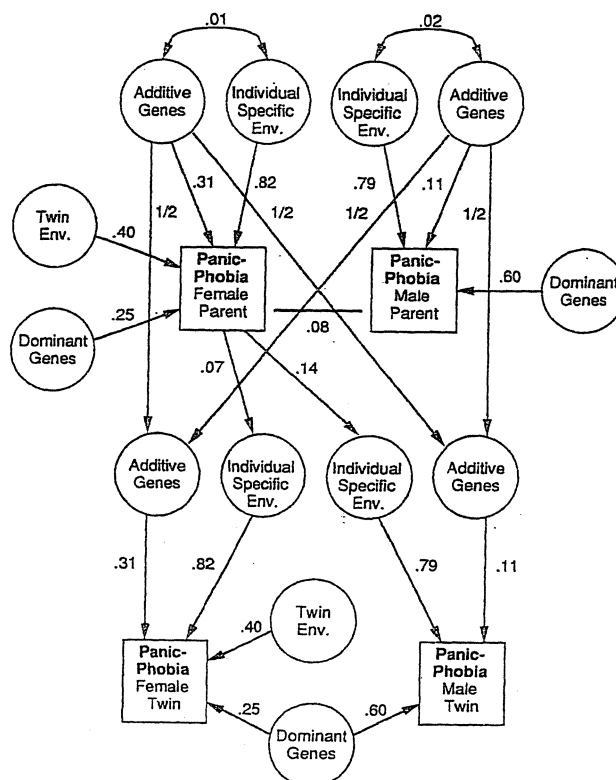
Fig. 2. The best-fitting model for self-report symptoms of panic–phobia from the AARP sample as depicted in a pair of DZ opposite-sex twins and their parents. This model suggests that familial resemblance for symptoms of panic–phobia is due to additive genes, dominance genes, assortative mating, maternal VCT, and special twin environment in females only. Although the same genetic factors influenced both genders, dominant genes had a greater impact on these symptoms in males and additive genes in females. For further explanation, see the text and the legend to Fig. 1.

Model Fitting in the AARP Sample Symptoms of Somatization

The details of model fitting in the AARP sample to the somatization factor are shown in Table VI. The full sex-dependent model fit the data quite well ($\chi^2 = 76.46$, df $= 63$, $p > .10$). Briefly, models without sex-independent parameters, assortative mating, genetic effects in general, or specifically scalar sex-dependent dominance genetic effects could be rejected against the full sex-dependent model. However, models without familial-environmental effect, nonscalar sex-dependent additive or dominance genetic effects, or scalar sex-dependent additive genetic effects could not be rejected.

As shown in Fig. 3 and Table V, the best-fitting model for somatization in the AARP sample (model XII; $\chi^2 = 95.65$, df $= 76$, $p = .063$) was

relatively simple and required (i) sex-independent additive genetic and individual specific environmental factors, (ii) scalar sex-dependent dominance genetic factors, and (iii) assortative mating. This model estimated the total heritability for these symptoms to be higher in males (48.8%) than in females (35.8%), with dominance genetic effects again accounting for a majority of the genetic variance.

Replication in the Virginia Sample

We applied the best-fitting model from the AARP sample for both of the symptom factors to the Virginia sample. The major results from these models are shown in Table V. The best-fitting model for the panic–phobia symptoms in the

Table V. Proportion of Total Variance Accounted for by Genetic and Environmental Factors for the Best-Fitting Models for Self-Report Symptoms of Panic–Phobia and Somatization in the Entire AARP and Virginia Twin-Family Samples[a]

| | Panic–phobia | | | | Somatization | | | |
| | Male | | Female | | Male | | Female | |
	AARP	VA	AARP	VA	AARP	VA	AARP	VA
Total genetic	37.8	25.8	16.1	15.3	48.8	27.9	35.8	25.1
Additive	1.3	11.1	9.7	1.6	15.4	12.5	15.4	12.5
Dominance	36.5	14.7	6.3	13.7	33.4	15.4	20.4	12.5
Total environmental	61.8	74.4	83.3	84.7	51.2	72.1	64.2	74.9
Total familial	1.2	0.1	16.5	6.0	0	0	0	0
Twin	0	0	16.2	6.0	0	0	0	0
Sibling	0	0	0	0	0	0	0	0
Mat. VCT	1.2	0.1[b]	0.3	0.0	0	0	0	0
Pat. VCT	0	0	0.0	0.0	0	0	0	0
Total nonfamilial	60.6	74.3	66.8	78.7	51.2	72.1	64.2	74.9
Total GE cov	0.4	0.0	0.6	0.0	0.0	0.0	0.0	0.0
Assortative mating	0.08	0.15	—	—	0.10	0.19	—	—

[a] AARP indicates American Association of Retired Persons sample; VA, Virginia sample; GE cov, genotype–environment covariance; VCT, vertical cultural transmission; mat, maternal; pat, paternal. 0 = fixed at zero.
[b] Path estimates were negative.

Table VI. Model Fitting for Self-Report Symptoms of Somatization in the AARP Sample

Model	χ^2	df	Tested against model	Accepted/ rejected	Description
I	76.46	63	—	—	Full sex dependent
II	98.87	74	I	R	Full sex independent
III	108.25	64	I	R	No assortative mating
IV	89.88	73	I	A	No familial-environmental effects
V	109.68	69	I	R	No genetic effects
VI	90.86	66	I	R	No dominance genetic effects
VII	76.47	64	I	A	No nonscalar sex-dependent additive genetic effects
VIII	89.88	74	—	—	No familial-environmental effects, no nonscalar sex-dependent additive genetic effects
IX	91.08	75	IX	A	No nonscalar sex-dependent dominance genetic effects
X	103.78	76	IX	R	No scalar sex-dependent dominance genetic effects
XI	92.96	75	IX	A	No scalar sex-dependent additive genetic effects
XII[a]	95.65	76	IX	A	Model IX + no nonscalar sex-dependent dominance or scalar sex-dependent additive genetic effects

[a] Best-fit model, which includes (i) sex-independent additive genetic and individual specific environmental factors, (ii) scalar sex-dependent dominance genetic factors, and (iii) assortative mating.

AARP sample produced a relatively poor fit in the Virginia sample ($\chi^2 = 50.70$, df = 24, $p < .005$). However, so did the full model ($\chi^2 = 41.84$, df = 15, $p < .001$) and the best-fit AARP model could not be rejected against the full model in the Virginia sample ($\chi^2 = 8.86$ df = 9, NS). The results from the Virginia sample replicated several key aspects of the AARP results: (i) a higher heritability in males than in females, (ii) more evidence for familial-environmental effects (i.e., special twin environment) in females than in males, and (iii) a greater importance of dominance vs. additive genetic effects. However, several notable differences between the two samples exist. First, the estimated variance due to familial-environmental factors in females was much lower in the Virginia (6.0%) than in the AARP (16.5%) sample. In particular, in females, the special twin environment in the
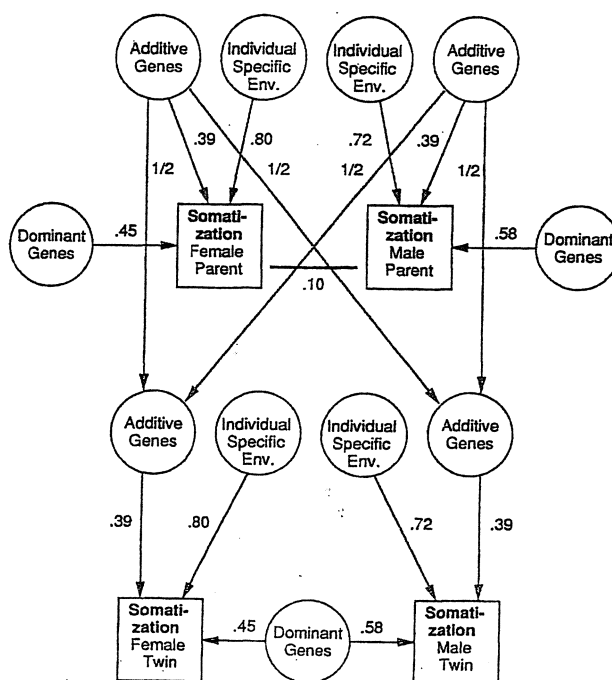
Fig. 3. The best-fitting model for self-report symptoms of somatization from the AARP sample as depicted in a pair of DZ opposite-sex twins and their parents. This model suggests that familial resemblance for symptoms of somatization is due solely to additive and dominance genes and assorative mating. Although the same genetic factors influenced both genders, dominant genes had a greater impact on these symptoms in males than in females, while additive genes had the same impact in both sexes. For further explanation, see the text and the legend to Fig. 1.

Virginia sample accounted for only 6% of the variance in self-report symptoms of panic–phobia (vs. over 15% in the AARP sample). Second, the Virginia sample did not replicate the evidence for maternal VCT found in the AARP sample, as in the Virginia sample this path was small and *negative* (−0.03).

For the symptoms of somatization, the best-fitting model from the AARP sample fit moderately well in the Virginia sample ($\chi^2 = 46.52$, df = 28, $p = .02$). This model differed marginally in fit from the full model ($\chi^2 = 6.42$, df = 2, $p = .04$), which itself did not produce an excellent fit to the data ($\chi^2 = 40.10$, df = 26, $p = .04$). Compared to the AARP sample, heritability of the symptoms of somatization is substantially lower in the Virginia sample in males (28 vs. 49%) and modestly lower in females (25 vs. 36%). While the additive genetic effects were of similar magnitude in the two samples, estimates of dominance genetic variation were about twice as great in both sexes in the AARP vs. the Virginia sample.

Analysis of Twins Only

To compare results obtained by the twin-family design to those that would have been obtained had we restricted our sample to twins, we performed model-fitting to only the twins from the larger AARP sample (details available on request). The parameter estimates from the best-fitting models are shown in Table VII. Heritability estimates from twins alone were very similar to those obtained from the entire twin-family sample for symptoms of panic–phobia in males (41.0 vs. 37.8%), somatization in males (49.6 vs. 48.8%), and somatization in females (36.2 vs. 35.8%). However, for symptoms of panic–phobia in females, heritability estimates were *much* higher from twins alone (35.1%) than from the entire twin-family sample (16.1%).

Adding Test–Retest Data to the Model

The results presented hitherto reflect the sources of variance for self-report psychiatric

Table VII. Proportion of Variance Accounted for by Genetic and Environmental Factors for the Best-Fitting Models for Self-Report Symptoms of Panic–Phobia and Somatization in the Twins from the AARP Sample[a]

	Panic–phobia		Somatization	
	M	F	M	F
Total genetic	41.0	35.1	49.6	36.2
Additive	3.4	35.1	21.1	36.2
Dominance	37.6	0	28.5	—
Total environmental	59.0	64.9	50.4	63.8
Total familial	0	0	0	0
Total nonfamilial	59.0	64.9	50.4	63.8

[a] M, male; F, female.

symptoms as assessed on one occasion. Because of previous evidence that self-report psychiatric symptoms are relatively stable over time (Duncan-Jones et al., 1990), it is of interest to determine the impact on our heritability estimates of removing measurement "error" and short-term fluctuation in symptom scores from our model. In so doing, we can examine the degree to which genetic factors are responsible for the proportion of variance in the SCL scores that is stable over time.

As outlined in Table VIII, the test–retest correlation for both symptom factors in the AARP and Virginia samples ranged from +0.51 to +0.63 over a mean 14-month period. By including these data to our best-fitting models for each symptom factor, we estimated that genetic factors accounted for about 50% or more of the stable variance for self-report psychiatric symptoms in both samples, with the exception of symptoms of panic–phobia in women.

COMMENT

Using mailed self-report questionnaires, we obtained self-report symptoms of anxiety in two large samples of twins and their families. We report here our attempt to understand the sources of familial resemblance for these self-report symptoms. We examine our major results in turn.

Factor Analysis

Although items were chosen from four SCL subscales (and sleep items), only three could be meaningfully identified in our sample. The original

depression, phobic anxiety, and somatization subscales of the SCL could be easily identified in our factor analysis, but the original SCL anxiety subscale could not be recovered. Neither increasing the number of extracted factors nor using an orthogonal rotation led to the emergence of a coherent anxiety factor. Our results are similar to those found by Lipman et al. (1979), who, using the full 90-item version, could not identify a meaningful anxiety factor but found the items split largely between a phobic–anxiety and what they called an agitated depression factor. The three identified factors were stable across samples and genders.

Twin-Family Analysis—Symptoms of Panic–Phobia

The results of model fitting with symptoms of panic–phobia were relatively complex. While the same genetic factors influenced males and females, the impact of dominance genetic factors was much greater in males than in females in the AARP sample. Familial-environmental factors were significant for symptoms of panic–phobia and were much more important in females than in males. In particular, we found evidence for a special twin environment for panic–phobia symptoms in females but not in males. Results in the Virginia sample were qualitatively similar to those found in the AARP data. However, the heritability differed considerably less across genders and the special twin environment for females was much less pronounced than in the AARP sample.

We are aware of three reports which have examined symptoms of anxiety in twins (Jardine et al., 1984; Clifford et al., 1984; MacKinnon et al., 1990). Using the anxiety subscale of the DSSI (Bedford et al., 1976), Jardine et al. (1984) found heritability estimates of +0.39 in females and +0.31 in males and no evidence for familial-environmental effects. Clifford et al. (1984), using the anxiety subscale of the Middlesex Hospital Questionnaire (Crown and Crisp, 1966), found that, under a variety of assumptions, heritability ranged from 19 to 50% and was higher in females than males. Of interest, they found evidence for a special twin environment for symptoms of anxiety. Mackinnon et al. (1990) found that in females, the anxiety subscale of the GHQ (Goldberg, 1978) could be explained by only genetic effects, with a heritability of 43%, and individual specific envi-

Table VIII. Test–Retest Correlation of Self-Report Symptoms of Panic–Phobia and Somatization and Heritability Estimates for These Symptoms Removing the Effects of Error of Measurement and Short-Time Fluctuation[a]

	AARP				Virginia		
	Reliability		Heritability[b]			Heritability[b]	
	M (*n*=1220)	F (*n*=2745)	M	F	Reliability[c] (*n*=1433)	M	F
Panic–phobia	0.51	0.63	72.9	24.0	0.54	47.1	29.8
Somatization	0.57	0.63	85.8	56.8	0.53	51.9	48.0

[a] M, male; F, female.

[b] Proportion of variance in the stable component of self-report symptoms due to additive and dominance genetic factors, as assessed using the previous best-fit model.

[c] Available only on females.

ronment. However, in his male sample, the best-fitting model was entirely environmental, with familial environment accounting for 41% of the variance.

It is difficult to compare our results with these previous studies because of differences in the nature of the symptoms assessed (i.e., phobic and panic symptoms vs. general "anxiety" symptoms). Furthermore, Martin *et al.* (1988), in the same Australian twin data set as that used by Jardine *et al.* (1984), found that symptoms of panic may be shaped by unique genetic influences which do not influence other symptoms of anxiety.

Somatization

The best-fitting model for self-report symptoms of somatization in the AARP sample included only additive and dominance genetic factors which influenced males more than females, individual specific environment and assortative mating. In the AARP sample, heritability estimates were relatively high in males (49%) and also substantial in females (36%). The main features of the results were replicated in the Virginia sample, although heritability estimates were lower and more similar in the two sexes. We are unaware of any previous study of self-report symptoms of somatization in a genetically informative population.

Additive vs. Dominance Genetic Variance

The total heritability of the symptom factors estimated in the AARP and Virginia samples was

more similar than was the specific proportion of variance due to additive vs. dominance genetic effects. These results suggest that, compared to our other findings, less confidence can be placed in our partitioning of the total genetic variance into additive and nonadditive components. The same pattern of results was seen with the depression factor (Kendler *et al.*, 1994). These results are not entirely surprising, as in twin and twin-family designs the estimates of additive and dominance effects are substantially correlated and can be difficult to resolve clearly, even with large samples (Eaves, 1972; Martin *et al.*, 1978; Neale *et al.*, 1994).

An Evaluation of the Twin Method in Psychiatric Genetics

One major use of the twin-family method is to determine whether results obtained in twins can be extrapolated to other more common family relationships. We were therefore interested in determining whether the addition of large samples of nontwin relatives would change the results obtained from twins alone. Our findings suggest that with respect to the estimation of total heritability and the detection of familial-environmental factors, the answers obtained from twins alone agreed closely with those obtained from the inclusion of large numbers of nontwin relatives with one major exception. In general, our results provide important evidence for the validity of the twin method in psychiatric research. However, the results for symptoms of panic–phobia in females are sobering, as they suggest that twin studies can overestimate her-

itability levels, particularly when special twin environmental factors may be operative.

Psychiatric Symptoms and Family Environment

Because of its large size and variety of family relationships, this sample provides one of the best available opportunities, in a genetically informative design, to detect an impact of family environment on psychiatric symptoms. With the notable exception of symptoms of panic–phobia in females, however, we failed to detect significant familial-environmental effects on symptoms of anxiety, and the same pattern was seen with depressive symptoms in this sample (Kendler et al., 1994). Our findings are consistent with the results of a range of behavior genetic studies (Plomin and Daniels, 1987; Eaves et al., 1989) which suggest that environmental effects on most behavioral traits arise from environmental experiences not shared by other family members but inconsistent with the claim that parental rearing behavior, at least insofar as it is shared by siblings, plays a major role in the etiology of anxiety disorders (Parker, 1981).

The Role of Genetic Factors in Stable Self-Report Symptoms

In addition to cross-sectional assessments of self-report psychiatric symptoms on twins and their relatives, we also had longitudinal data on a large sample of twins from both the AARP and the Virginia samples. As suggested previously (Duncan-Jones et al., 1990), scores for the same individual were substantially correlated over a 1- to 2-year period for both symptom factors in both samples. While intended by its developer to assess psychiatric "state" (Lipman et al., 1979), the SCL clearly is, at least in part, a reflection of "trait-like" characteristics.

The addition of these test–retest data to our model fitting allowed us to address an additional interesting question—the role of genetic factors in the temporal stability of self-report symptoms. Our results suggest that the stable component of self-report symptoms is due, to a substantial degree, to genetic factors. These results suggest that a large proportion of what is estimated as individual-specific environment in cross-sectional evaluations of

psychiatric symptoms appears to be due to short-term fluctuations in symptom scores.

Limitations

The results of this report should be interpreted in the context of six potentially significant limitations. First, because our results are based solely on symptoms reported by individuals in a mailed questionnaire, they should not be assumed to apply to clinically defined syndromes such as panic disorder and generalized anxiety disorder.

Second, the AARP sample, the larger of our two samples and the primary one analyzed here, was a volunteer sample and demonstrates all the typical characteristics thereof: a high average educational level, a preponderance of females, and a substantial excess of MZ over DZ twins (Lykken et al., 1978). While most theoretical analyses suggest that volunteer bias is more likely to diminish than increase heritability estimates (Martin and Wilson, 1982; Neale et al., 1989), it is still possible that the higher heritability estimates in the AARP versus the population-based Virginia sample could result from the greater volunteer bias in the former versus the latter sample.

Third, all our analyses were carried out on obliquely derived factors that most accurately reflect the true factor structure within our sample. How different might our results have been if the more traditional orthogonal factors were used instead? Orthogonal factors looked quite similar to the oblique factors shown in Table III, except that, as expected, cross-factor loadings were higher. While the overall patterns of the best-fitting models were similar using the two rotations, heritabilities were moderately higher with the oblique vs. orthogonal rotation.

Fourth, although our analytic model assumed that spousal resemblance for self-report symptoms results from "phenotypic" assortative mating, such resemblance could be due, instead, to spousal interaction or social homogamy (Heath and Eaves, 1985; Eaves et al., 1984; Heath, 1987). While we cannot definitively rule out this possibility, the available evidence supports the validity of our assumption. Most models of spousal interaction would predict a significant negative correlation between duration of marriage and spousal differences in symptom scores. However, for symptoms of

both panic–phobia and somatization, these correlations were quite low and positive (+0.052 and +0.048, respectively). Assortment based on social homogamy would predict that the correlation in symptom scores between a twin and his/her cotwin's spouse should be similar in MZ and DZ pairs, while phenotypic assortment predicts the former to be greater. The pattern observed (+0.08 and −0.05, respectively, for panic–phobia and +0.07 and +0.03, respectively, for somatization) is as predicted by phenotypic assortment.

Fifth, these data may not provide a strong test for environmental transmission of psychiatric symptoms within families. Parents with many symptoms of panic and phobia, for example, may influence their children's level of such symptoms only when the children are young and cohabiting with their parents. Such effects would almost certainly go undetected in these data, which can examine only the effects of family environment that *endure* into adulthood.

Finally, a critical assumption of our models was that genetic factors that influence self-report psychiatric symptoms are stable in their effect throughout adulthood. However, gene expression can be quite variable over the life cycle, with certain genetic systems "switching" "on" and "off" (Wetherall and Clegg, 1981; Eaves *et al.*, 1986). We tested the assumption of genetic temporal stability in pairs of nontwin siblings from the AARP sample and found that sibling resemblance for symptoms of panic–phobia and somatization was independent of their age difference. These results suggest that, at least over the age differences commonly seen in sibships, genetic influences on self-report psychiatric symptoms are temporally stable. However, it cannot be ruled out that the higher heritabilities found in the older AARP sample may result in part from a trend for the heritability of self-report psychiatric symptoms to increase with age.

ACKNOWLEDGMENTS

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Edited by Peter McGuffin