ORIGINAL ARTICLE

The Etiology of Phobias

An Evaluation of the Stress-Diathesis Model

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Background: We evaluated for phobias the prediction of the stress-diathesis model that the magnitude of stress at onset is inversely proportional to the level of underlying diathesis.

Methods: In more than 7500 twins from a population-based registry, we assessed the personality trait of neuroticism—as an index of phobia-proneness—and the lifetime histories of 5 phobia subtypes (agoraphobia, social, animal, situational, and blood or injury) and their associated irrational fears. Interviewers classified the mode of acquisition of the fear in phobic twins into 5 possible categories: trauma to self (further divided by severity), observed trauma to others, observed fear in others, taught by others to be afraid, and no memory of how or why fear developed. Analyses were conducted by logistic regression and analysis of covariance.

Results: The mode of acquisition had moderate test-retest reliability and differed meaningfully across phobia subtypes. None of the 3 tests of the stress-diathesis model was confirmatory: (1) the risk of phobias was not elevated in co-twins of twins who had no memory of their mode of acquisition, (2) the risk of phobias was not decreased in co-twins of twins who had severe trauma to self, and (3) no significant relationship, in phobic twins, was found between levels of neuroticism and mode of acquisition.

Conclusions: These results are inconsistent with the traditional etiologic theories for phobias, which assume conditioning or social transmission. However, they are compatible with nonassociative models, which postulate that the vulnerability to phobias is largely innate and does not arise directly from environmental experiences. The stress-diathesis model may not be an appropriate paradigm for phobic disorders.

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AS PROPOSED by the "stress-diathesis" model,[1] most psychiatric disorders are thought to arise as a result of environmental adversity experienced by predisposed individuals. The goal of this report is to evaluate the validity of this model for phobias.

The stress-diathesis model predicts that, among affected individuals, an inverse relationship exists between the level of "diathesis" (or liability) and the level of onset-related environmental trauma. Affected individuals whose onset was associated with high levels of trauma should, on average, have lower levels of disease liability than affected individuals with no or little trauma associated with onset.

Expanding on the multiple pathways model of Rachman,[2] recent studies[3-11] have suggested 5 modes of acquisition (MOAs) for phobias and/or their associated irrational fears: (1) traumatic event occurring to self, (2) observation of traumatic event to others, (3) observation of fear or avoidance in others, (4) taught to be afraid, and (5) no memory of how or why the fear developed (commonly indicated by the response of phobic patients, "I've just always been afraid of X"). We abbreviate these as *trauma to self*, *trauma to others*, *observed in others*, *taught fear*, and *no memory*, respectively.

The hypothesis that we sought to evaluate is illustrated in the **Figure**. We assumed that these MOAs can be roughly ranked as a function of the associated level of environmental trauma. In particular, we postulated that those with no memory of a traumatic event tend to have high levels of endogenous liability (point A), while those who report the onset of fear associated with a major trauma to self will have low average liability (point F). Without strong prior evidence, we suggest that the other MOAs lie somewhere between these 2 extremes (points B, C, D, and E).

SUBJECTS AND METHODS

SAMPLE

The data used in this report derive from an ongoing study of white twin pairs from the Virginia Twin Registry,[24,25] a population-based registry formed from a review of all birth certificates in the Commonwealth of Virginia. Female-female twin pairs born between 1933 and 1972 were initially ascertained through mailed surveys to female twin pairs in the registry, the response to which was approximately 64%. Twins were then interviewed face to face, at which time our refusal rate was approximately 12%. For the fourth interview wave in this project, 2228 members of female-female pairs from the Virginia Twin Registry were eligible to participate in a structured telephone interview. These twins were unselected except that they had participated in previous face-to-face interviews in this project. Of these 2228 twins, 1937 were successfully interviewed in 1995 to 1997. At the fourth wave, the mean (±SD) age and years of education of the sample were, respectively, 36.3±8.2 years and 14.3±2.2 years. To assess test-retest reliability, 190 randomly selected twins were reinterviewed 4.3±1.5 weeks after their initial interview.

Male-male and male-female twin pairs were selected from the birth years of the registry of 1940 to 1974.[26] Of 9417 eligible individuals for the first wave, 6814 (72.4%) completed the interview. At least 1 year after the completion of the first-wave interview, which was performed, in most instances, by telephone, we contacted the twins again and attempted to schedule a second-wave interview. The number of subjects eligible for wave 2 interviews included the 6814 with complete wave 1 interviews as well as 3 subjects interviewed at wave 2 who were eligible but not interviewed at wave 1. Where possible, this interview was completed face to face (79.4% of sample). Of the 6817 eligible individuals for the wave 2 interview, 5629 (82.6%) were successfully interviewed. At the second wave, the mean (±SD) age and years of education of the sample were, respectively, 37.0±9.1 and 13.6±2.6 years. To assess test-retest reliability in this sample, 195 randomly selected twins were reinterviewed 4.4±1.3 weeks after their initial interview.

All interviews were conducted blind to information about the co-twin. These projects were approved by our local institutional review board. Subjects were informed about the goals of the study and provided verbal consent before telephone interviews and written informed consent before face-to-face interviews and collection of DNA samples. Zygosity was determined by algorithms that included photographs, anthropometric data, and questions about physical similarity and frequency of being mistaken for one another as children, and DNA analysis.[27]

ASSESSMENTS

We assessed a lifetime history of phobias with an adaptation of the Phobic Disorders section of the Diagnostic Interview Schedule, version III-A.[17,28] We assessed 22 specific irrational fears (**Table 1**) and also asked respondents, "Is there anything else you've been unreasonably terrified to do or be near?" If any phobia described in response to this question best belonged with 1 of the 5 specific subtypes, it was so treated.

In the Diagnostic Interview Schedule, to be considered a phobia, the irrational or unreasonable fear must result in (1) seeing a physician, (2) taking medications, or (3) reporting the fear or its avoidance "interfered with life or activities a lot." Given the low and variable rates of treatment seeking for phobias,[29] we defined phobias solely through a modification of the third criterion: objective behavioral impact of the fear on respondent behavior. In contrast to the Diagnostic Interview Schedule, where the respondent makes the judgment about fear-associated interference, in our interview, the interviewer—who had either a master's degree in a mental health–related discipline or a bachelor's degree and 2 years of clinical experience—made this assessment.

For each fear that was judged to be associated with impairment, the interviewers asked, "Thinking back, how did this unreasonable fear begin?" If the initial response was no memory, they were instructed to ask, "Was there a specific event or situation in which you were frightened or hurt? Did the fear begin when you saw others being afraid? Did someone teach you to be afraid?"

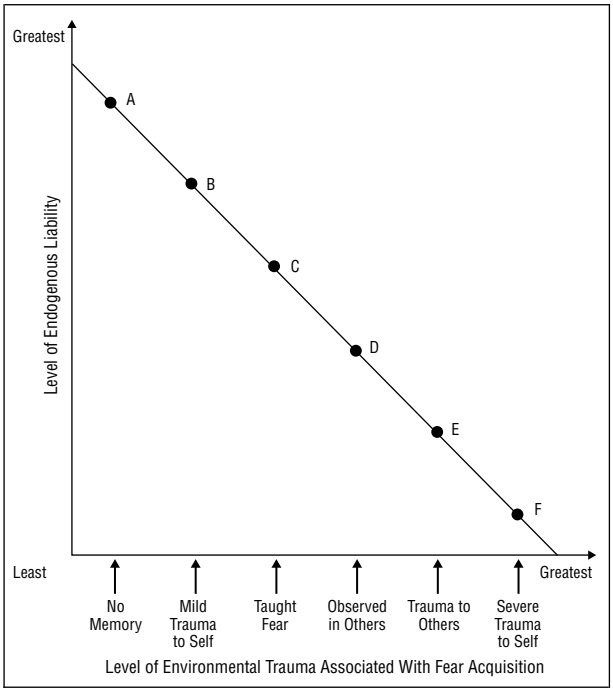
The interviewers coded the response of the twin into 1 of the 5 MOAs outlined above. If the twin reported phobia onset associated with a traumatic event to self, the interviewer asked for details about the event and then rated it as severe (eg, in plane crash with several fatalities, severely mauled by large dog), moderate (eg, bitten by a nonpoisonous snake, locked in a dark closet for a significant period), or mild (eg, found a spider in a sleeping bag, fall from tree without injury). Neuroticism was measured with 12 items empirically chosen from the Eysenck Personality Questionnaire.[22,30] In our female twins, the test-retest reliability of this measure over 17 and 61 months was +0.69 and +0.63, respectively.

STATISTICAL ANALYSIS

Reliability was assessed by means of the unweighted κ coefficient[31] and is reported as $\kappa \pm$ SE. The association between MOA and phobia subtypes was assessed by standard χ^2 analysis. We assessed the relationship between MOA in one twin and the risk of phobia in the co-twin by logistic regression, controlling for zygosity, age at interview, sex of co-twin, and study (female-female vs male-male/male-female). We corrected for the correlational structure of our data, which includes both the correlation among multiple phobias within the same individual and the correlation within twin pairs, using independent estimating equations[32] as implemented in the SAS procedure GENMOD.[33] Differences in the level of the personality trait neuroticism across groups were assessed by analysis of covariance with the same set of covariates. In these analyses of covariance only, the use of independent estimating equations resulted in a substantial loss of degrees of freedom, and in 2 of the analyses did not converge to a stable solution. All of these results were rerun without the independent estimating equations, with only modest changes. We therefore present these more stable results herein.

In a large epidemiologic twin sample, we evaluated 3 predictions from the stress-diathesis model applied to phobias:

1. Given the importance of familial-genetic factors in the etiology of phobias and irrational fears,[12-20] in twins with a lifetime history of phobias, the risk of fears and



A prediction of the stress-diathesis model. In affected individuals, the stress-diathesis model predicts there will be an inverse relationship between the level of endogenous disease liability (y-axis) and the level of environmental trauma associated with fear acquisition (x-axis). We postulate that the characterized modes of acquisition of the phobia, listed on the x-axis, can be roughly ranked as a function of the associated level of environmental trauma. Point A is associated with the lowest level of environmental trauma because it reflects the environmental stress of individuals who have no memory of any event association with fear acquisition (no memory). According to the stress-diathesis model, these individuals ought, on average, to have very high levels of endogenous liability; hence, point A is the highest point on the y-axis. Point F is associated with the highest level of environmental trauma because it reflects the environmental stress of individuals who recalled their phobia onset associated with a personal experience of a severely traumatic event (severe trauma to self). According to the stress-diathesis model, these individuals ought, on average, to have quite low levels of endogenous liability. Hence, point F reflects the lowest point on the y-axis. Without strong prior evidence, we suggest that the other modes of acquisition probably lie somewhere between these 2 extremes (and are presented by points B, C, D, and E in the Figure).

phobias in their co-twins will be highest in twins with the lowest level of environmental trauma.

2. Among phobic twins with an MOA of trauma to self, an inverse relationship will be seen between the severity of the trauma and the risk of fears and phobias in their co-twin.

3. The personality trait of neuroticism—which reflects predisposition to negative emotionality—is significantly related to the risk of phobias[21-23] and can therefore serve as a quantitative index of phobia-proneness. The stress-diathesis model then predicts that (1) levels of neuroticism will be highest in phobic twins whose onset was associated with the lowest levels of trauma and (2) among phobic twins who report onset associated with trauma to self, an inverse relationship will be seen between level of trauma and level of neuroticism.

RESULTS

MODE OF ACQUISITION

Our sample contained 7545 interviewed twins with complete data on fears and phobias. Of those, 1967 (26.1%) reported one or more phobias. These 1967 individuals reported a total of 3374 individual impairing fears that met criteria for phobias on which we had information on MOA. The number of individual fears with impairment reported ranged from 1 to 13, with a mean (SD) of 1.9 (1.4). When asked about the MOA of these fears, no memory was the most common response (48.8%), followed by trauma to self (35.7%), taught fear (7.6%), observed in others (4.1%), and trauma to others (3.9%).

Substantial differences in mode of acquisition were observed in individual fears and by phobia subtypes (Table 1). The distribution of the 5 MOAs in the 5 phobic subtypes was highly nonrandom ($\chi^2_{16}=360.9$, $P<.001$).

"No memory" was the response in more than 50% of subjects for all the agoraphobic fears and all but one of the social and situational fears, but none of the animal or blood/injury fears. By contrast, trauma to self was reported by more than 40% of the subjects for all of the animal fears and for fear of other closed places, needles/injections, and dentists/hospitals. Trauma to others was reported by more than 10% of the sample only for 2 blood/injury fears: fear of blood and fear of diseases. "Observed in others" was given most commonly for fear of bats, and here it was endorsed by only 8.1% of the subjects. "Taught fear" was reported by more than 10% of the sample for public bathrooms, fear of mice, snakes, bats, and other animals, and fear of airplanes and diseases.

Of the 385 twins who completed test-retest interviews, 56 reported fears with impairments in the same phobia subtype on both occasions. Reliability for our 5 categories of MOA was moderate ($\chi^2_{16}=53.5$, $P<.001$; $\kappa=0.50\pm0.09$). Only 14 twins reported phobias of the same subtype due to trauma to self on both occasions. The reliability of the severity ratings in this small sample was modest ($\kappa=0.38\pm0.22$).

The sample contained 106 twin pairs concordant for the same phobia subtype. No significant twin resemblance was observed in MOA in these pairs ($\kappa=0.11\pm0.07$). Furthermore, no significant excess was seen of pairs where both reported trauma to self (as would be expected if both twins developed a phobia in reaction to a shared traumatic experience) (observed, 14 pairs; expected, 12.2 pairs; cell $\chi^2=0.27$) or pairs where one twin reported trauma to self and the other twin reported trauma to others (observed, 5 pairs; expected, 3.4 pairs; cell $\chi^2=0.81$). The resemblance for MOA was similar in monozygotic ($\kappa=0.12\pm0.08$) and dizygotic ($\kappa=0.09\pm0.09$) pairs.

RELATIONSHIP BETWEEN MOA AND RISK IN CO-TWIN

No Memory vs Other MOAs

Our first test of the diathesis-stress model applied to phobias examined the risk of the same phobia subtype or of any phobia in the co-twins of 2 groups of phobic twins: (1) those who reported a specific MOA for their fear (ie, trauma to self, trauma to others, observed in others, or taught fear) and (2) those who reported no memory of their MOA. When adjusted for zygosity, sex, age at interview, and the correlational structure of the data, we found no signifi-

Table 1. Mode of Acquisition of Individual Phobias

Fear	No. of Subjects	Mode of Acquisition, %*				
		Trauma to Self	Trauma to Others	Observed in Others	Taught Fear	No Memory
Agoraphobia						
Out of house alone	118	35.6	3.4	0.8	5.9	54.2
Crowds	271	23.2	1.5	1.1	4.1	70.1
Open spaces	26	26.9	3.8	3.8	3.8	61.5
Any agoraphobia	415	27.0	2.2	1.2	4.6	65.1
Social						
New people	135	20.0	0.0	4.4	6.7	68.9
Speech	383	26.4	0.5	2.9	1.0	69.2
Public bathrooms	87	12.6	2.3	5.7	35.6	43.7
Eating in public	57	26.3	5.3	1.8	7.0	59.6
Any social	662	23.3	1.1	3.5	7.3	65.0
Animal						
Spiders	137	41.6	1.5	3.6	8.8	44.5
Bugs	64	40.6	3.1	6.3	6.3	43.8
Mice	78	48.7	2.6	2.6	11.5	34.6
Snakes	267	40.8	4.9	6.4	13.9	34.1
Bats	37	62.2	5.4	8.1	18.9	5.4
Other animals	141	67.4	5.7	4.3	11.3	11.3
Any animal	724	48.1	4.0	5.1	11.6	31.2
Situational						
Tunnels	81	22.2	1.2	3.7	4.9	67.9
Other closed places	238	46.2	0.8	3.4	1.7	47.9
Bridges	104	26.9	3.8	5.8	9.6	53.8
Airplanes	207	23.2	4.8	6.3	15.5	50.2
Other high places	392	33.2	2.3	6.9	3.6	54.1
Any situational	1022	32.7	2.5	5.6	6.3	52.9
Blood/injury						
Blood	71	31.0	19.7	0.0	7.0	42.3
Needles/injections	175	49.1	3.4	4.6	2.9	40.0
Dentists/hospitals	204	66.2	3.4	1.5	3.4	25.5
Diseases	102	14.7	32.4	3.9	22.5	26.5
Any blood/injury	552	46.7	10.9	4.1	7.6	48.8

*Because of rounding, percentages may not total 100.

cant difference in risk for phobias in the co-twins of these 2 groups of phobic twins (**Table 2**). This pattern was seen when we examined individual phobia subtypes or all phobias. Contrary to expectation, in the entire sample of phobic twins, the risk of any phobia was nonsignificantly lower (odds ratio [OR] = 0.86) in co-twins of twins who reported no memory of their MOA vs those who recalled a specific MOA. We repeated these analyses (data not shown) for each of the 22 individual fears. Significant effects were found for 2 specific fears, a result that would occur at least 30% of the time by chance alone.[34] The co-twins of twins with a phobia of using public bathrooms (OR, 0.19; 95% confidence interval [CI], 0.04-0.97) and snakes (OR, 0.35; 95% CI, 0.13-0.98) had a lower risk of phobia if the twin had no memory of the MOA vs recalling a specific MOA.

We then repeated these analyses predicting irrational fear—rather than phobia—in the co-twin. As seen in Table 2, again no significant results were found. Contrary to prediction, lack of memory of the MOA for fears in a phobic twin did not predict an increased risk of an irrational fear in the co-twin.

Mild vs Moderate or Severe Trauma to Self

Among all those who reported trauma to self as their MOA, the level of severity of trauma was rated as follows: mild, 64.0%; moderate, 26.5%; and severe, 9.5%. We combined moderate and severe into a single category and compared the risk for phobias and fears in the co-twins of those twins who reported their fear onset after mild vs moderate or severe traumas. The results varied across phobia subtypes (**Table 3**). No significant effect of level of trauma on risk of phobia in co-twins was seen for agoraphobia, social phobia, and blood/injury phobia. However, contrary to our prediction, for animal, situational, and any phobia, the risk was significantly higher in the co-twins of twins whose onset of fear was associated with moderate or severe trauma. When we considered irrational fears in the co-twin, however, no significant effects were seen. That is, the level of trauma associated with the acquisition of fear in these phobic twins was unrelated to the risk of an irrational fear in their co-twins (Table 3).

No Memory vs Moderate or Severe Trauma to Self

As a final test of the hypothesis, we compared the risk of phobias and fears in the 2 groups with what we predicted to be the most divergent level of endogenous liability—those with no memory as their MAO vs those with trauma to self rated by the interviewers as either moderate or severe (**Table 4**). For agoraphobia, social phobias, and blood/injury phobias, no significant effects were

Table 2. Impact of a Specific Mode of Acquisition of Phobia vs No Memory on Risk of Phobias or Fears in the Co-twin

Phobia Subtype	No. of Subjects	Risk of Phobia in Co-twin*		Risk of Irrational Fear in Co-twin*	
		OR†	95% CI	OR†	95% CI
Agoraphobia	330	0.84	0.38-1.88	1.21	0.57-2.56
Social	519	1.05	0.54-2.06	1.10	0.72-1.68
Animal	579	0.62	0.22-1.73	1.08	0.70-1.68
Situational	810	0.61	0.37-1.03	0.74	0.53-1.03
Blood/injury	423	0.76	0.32-1.82	0.94	0.54-1.63
Any	2661	0.86	0.63-1.17	0.97	0.81-1.18

*Adjusted for zygosity, sex, age at interview, and the correlational structure of the data. OR indicates odds ratio; CI, confidence interval.

†Odds of having a phobia (or fear) in the co-twin of a phobic twin with no memory of mode of acquisition vs the co-twin of a phobic twin with a memory of a specific mode of acquisition.

Table 3. Impact of Severe or Moderate vs Mild Trauma to Self as Mode of Acquisition on Risk for Phobia and Irrational Fears in the Co-twin

Phobia Subtype	No. of Subjects	Risk of Phobia in Co-twin*		Risk of Irrational Fear in Co-twin*	
		OR†	95% CI	OR†	95% CI
Agoraphobia	85	3.95	0.40-39.28	2.09	0.35-12.45
Social	128	0.31	0.04-2.31	0.80	0.28-2.30
Animal	279	6.75	1.74-26.17	0.83	0.40-1.73
Situational	262	2.90	1.13-7.46	1.71	0.90-3.27
Blood/injury	197	1.10	0.44-2.75	1.24	0.57-2.67
Any	951	2.45	1.37-4.39	1.17	0.80-1.72

*Adjusted for zygosity, sex, age at interview, and the correlational structure of the data. OR indicates odds ratio; CI, confidence interval.

†Odds of having a phobia (or fear) in the co-twin of a phobic twin with a mode of acquisition of moderate or severe trauma to self vs the co-twin of a phobic twin with a mode of acquisition of mild trauma to self.

Table 4. Impact of No Memory vs Moderate or Severe Trauma to Self as the Mode of Acquisition of Phobia on Risk for Phobias or Fears in the Co-twin

Phobia Subtype	No. of Subjects	Risk of Phobia in Co-twin*		Risk of Irrational Fear in Co-twin*	
		OR†	95% CI	OR†	95% CI
Agoraphobia	267	1.37	0.52-3.60	0.89	0.34-2.33
Social	365	0.37	0.05-2.44	0.81	0.31-2.13
Animal	272	3.99	1.19-13.44	0.62	0.30-1.29
Situational	541	2.79	1.41-5.52	1.67	1.00-2.79
Blood/injury	213	1.33	0.38-4.68	1.01	0.46-2.23
Any	1658	1.72	1.11-2.68	0.98	0.71-1.35

*Adjusted for zygosity, sex, age at interview, and the correlational structure of the data. OR indicates odds ratio; CI, confidence interval.

†Odds of having a phobia (or fear) in the co-twin of a phobic twin with a mode of acquisition of moderate or severe trauma to self vs the co-twin of a phobic twin with no memory of a mode of acquisition.

seen. However, for animal phobia, situational phobia, and any phobia, the results were contrary to that predicted. The risk of phobias was significantly higher in the co-twins of those with an MOA of moderate or severe trauma than in the co-twins of those with no memory of an MOA. We repeated these analyses examining the risk of irrational fears in the co-twin. None of the results was significant.

NEUROTICISM AND MOA

Using logistic regression controlling for zygosity, sex, age at interview, interview form, and correlations within families, the level of standardized neuroticism strongly predicted risk of phobia (OR, 1.67; 95% CI, 1.58-1.77; $z=18.55$; $P<.001$). Levels of neuroticism significantly predicted all 5 phobia subtypes, with ORs ranging from 1.39 (95% CI, 1.29-1.51) for animal phobia to 2.36 (95% CI, 2.15-2.60) for agoraphobia.

Controlling for the same variables in an analysis of covariance, we found no significant relationship of neuroticism and MOA in those with a diagnosis of agoraphobia ($F_{4,348}=0.28$, $P=.89$), social phobia ($F_{4,564}=1.87$, $P=.11$), animal phobia ($F_{4,610}=1.65$, $P=.16$), situational phobia ($F_{4,872}=0.53$, $P=.71$), blood/injury phobia ($F_{4,442}=1.46$, $P=.21$), or any phobia ($F_{4,2872}=1.82$, $P=.12$).

Among phobic twins who reported trauma to self as the MOA, with the use of the same control variables, neuroticism was not significantly associated with severity of trauma for agoraphobia ($F_{2,89}=0.20$, $P=.82$), social phobia ($F_{2,132}=1.32$, $P=.27$), animal phobia ($F_{2,286}=0.11$, $P=.89$), or blood/injury phobia ($F_{2,203}=0.18$, $P=.84$). However, contrary to prediction, for both twins with situational phobias and twins with any phobia who reported trauma to self as the MOA, neuroticism was significantly and positively associated with level of trauma ($F_{2,276}=3.32$, $P=.04$, and $F_{2,104}=3.46$, $P=.03$, respectively). That is, in these analyses, neuroticism was highest in those who reported phobia onset associated with severe trauma and lowest in those who reported phobia onset associated with mild trauma.

Finally, we compared the level of neuroticism in the 2 groups of phobic twins that we expected to have the most divergent level of endogenous liability: those whose onset was associated with no memory vs moderate or severe trauma to self. Neuroticism did not differ significantly for any of the 5 phobia subtypes: agoraphobia ($F_{1,277}=0.05$, $P=.82$), social phobia ($F_{1,398}=2.04$, $P=.15$), animal phobia ($F_{1,279}=1.14$, $P=.29$), situational phobia ($F_{1,577}=3.18$, $P=.08$), or blood/injury phobia ($F_{1,213}=0.02$, $P=.88$).

COMMENT

The goal of this report was to evaluate the stress-diathesis model for the etiology of phobias. We wished to test the hypothesis that, in individuals with phobias, the degree of environmental stress associated with fear onset would be inversely related to the level of endogenous liability to phobia-proneness. We assessed "stress" by asking adult twins about how their unreasonable fear began. Many twins responded that they had no memory of any predisposing experiences, often stating that they had "just always felt afraid of X." We assessed the liability to phobias in 2 ways: indirectly through the risk of fears or phobias in their co-twins and directly by the personality trait of neuroticism.

All of our tests to verify the stress-diathesis model for phobias failed. Given the substantial evidence that heritable factors contribute to the liability to phobia or fear-proneness,[12-20] we first predicted that the risk of fears or phobias should be higher in phobic twins who had no recollection of any trauma for their MOA vs those who recalled some specific environmental precipitant. We found no such effect.

Second, we predicted that among individuals who reported fear onset associated with trauma to self, the greater the degree of trauma, the lower the level of risk for phobias in their co-twin. We found no such effect for any phobia, and for 2 subtypes (animal and situational) we found a significant effect in the opposite direction.

Third, we picked our 2 groups that, a priori, we predicted to have the highest and lowest levels of environmental stress associated with fear onset: those with moderate or severe trauma to self and those with no memory. The only significant effects found on risk of fears or phobias in the co-twin were again contrary to the prediction of the stress-diathesis model.

Fourth, using the personality trait of neuroticism as an index of liability to fear-proneness, we showed that in the entire sample this trait was strongly related to risk of phobias but did not discriminate between different MOAs among the phobic twins. Neuroticism was not, as predicted, higher in those with no memory as their MOA than in those whose phobia onset was associated with high levels of trauma. Again, the only significant effects found in these analyses were contrary to those predicted by the stress-diathesis model.

We see 3 plausible explanations for these findings. First, the stress-diathesis model may be correct but our measure of "stress" lacked sufficient reliability or validity to be useful. Skepticism about our measure is certainly warranted in that many years usually separated the onset of the fears from our assessment. Some of those reporting no memory might have had a highly traumatic experience that they subsequently repressed or simply forgot. However, MOAs assessed in our sample appear to have some face validity in that they differed meaningfully across the phobia subtypes in accord with previous literature.[3-11] Our test-retest data suggested at least moderate reliability for our measures of MOA. Furthermore, our interviewers were instructed to probe any initial response of "no memory." Finally, our sample size was large so that even if our assessment of stress were substantially error-prone, we would be likely to detect some effect.

The second plausible explanation is that the stress-diathesis model is correct but our measures of "diathesis" are invalid or unreliable. We consider this less likely, as the twin design is a powerful one and we have shown heritable components to phobias and their associated fears several times in this sample.[17,19,20] Neuroticism is also a well studied, heritable, and valid index of general emotionality.[22,35,36] Consistent with previous literature,[21,23] neuroticism was strongly related in our data to the risk of fears and/or phobias.

Third, the stress-diathesis model may be inapplicable to phobias. We consider this the most plausible explanation given the size of our sample and the consistently negative results of our analyses. Furthermore, this result is in accord with a growing body of data from both retrospective[8,10] and prospective[5,6,11] studies that suggest that most phobias are acquired nonassociatively (ie, without the involvement of learning). This theory suggests that the liability to phobias is innate, having arisen from evolutionary selection, and does not require environmental experiences to be manifest.[8,11]

If the stress-diathesis model for phobias is incorrect, 2 puzzling issues are raised. First, why do so many patients with phobias recall environmental experiences associated with their onset? Perhaps many phobia-producing experiences are so common that phobic individuals recall them in a "search after meaning." Alternatively, individuals might recall their first contact with the feared object as traumatic because the elicitation of the innate fear was itself stressful.

Second, why are monozygotic twins only moderately correlated for their liability to phobias, even when errors of measurement[19] are accounted for? Environmental variation of importance for phobias may reflect successful habituation experiences.[5,37] Alternatively, many environmental traumatic experiences may be nonspecific and unrelated to any specific phobic stimulus, increasing the liability to all phobias.[38] This hypothesis is supported by multivariate twin analyses of phobias in both female[17] and male[20] twins from the Virginia registry that found evidence of a single common factor of individual-specific environmental experiences that predisposed to all phobia subtypes.

Perhaps the most puzzling result was the evidence, found both with risk of phobia in co-twins and with levels of neuroticism, that the liability to phobia was highest rather than lowest in those whose onset was associated with moderate or severe trauma to self. This was inconsistent, found with some phobias and not others, and not found with risk of fears in the co-twin. The single traumatic phobia-producing event could have increased levels of neuroticism, but this would not explain the greater risk in co-twins. The risk in co-twins could be increased because the co-twins shared the traumatic event directly or indirectly with their twin, but we find no evidence of that. Could individuals with high liability select themselves into such traumatic events or recall them with a high likelihood? Might severe events inoculate against risk of phobias for individuals with low liability? Although highly speculative, consistent with the latter hypothesis are findings that falls resulting in injury between the ages of 5 and 9 years were associated with a reduced risk of fear of heights at age 18.[6]

Although the stress-diathesis model for phobias is conceptually appealing, 3 different attempts to validate its predictions in a large epidemiologic sample of twins all failed. These results, which suggest that the stress-diathesis model may not be an appropriate paradigm for most phobic patients, are more consistent with nonassociative models of phobia acquisition than with traditional etiologic theories involving conditioning or social transmission.

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REFERENCES

1. Monroe SM, Simons AD. Diathesis-stress theories in the context of life stress research: implications for the depressive disorders. *Psychol Bull*. 1991;110:406-425.
2. Rachman S. The conditioning theory of fear-acquisition: a critical examination. *Behav Res Ther*. 1977;15:375-387.
3. Ost LG, Hugdahl K. Acquisition of phobias and anxiety response patterns in clinical patients. *Behav Res Ther*. 1981;19:439-447.
4. Ost LG. Ways of acquiring phobias and outcome of behavioral treatments. *Behav Res Ther*. 1985;23:683-689.
5. Poulton R, Waldie KE, Craske MG, Menzies RG, McGee R. Dishabituation processes in height fear and dental fear: an indirect test of the non-associative model of fear acquisition. *Behav Res Ther*. 2000;38:909-919.
6. Poulton R, Davies S, Menzies RG, Langley JD, Silva PA. Evidence for a non-associative model of the acquisition of a fear of heights. *Behav Res Ther*. 1998; 36:537-544.
7. Merckelbach H, Arntz A, de Jong P. Conditioning experiences in spider phobics. *Behav Res Ther*. 1991;29:333-335.
8. Menzies RG, Clarke JC. The etiology of fear of heights and its relationship to severity and individual response patterns. *Behav Res Ther*. 1993;31:355-365.
9. Kleinknecht RA. Acquisition of blood, injury, and needle fears and phobias. *Behav Res Ther*. 1994;32:817-823.
10. Menzies RG, Clarke JC. The etiology of acrophobia and its relationship to severity and individual response patterns. *Behav Res Ther*. 1995;33:795-803.
11. Poulton RG, Menzies RG, Craske MG, Langley JD, Silva PA. Water trauma and swimming experiences up to age 9 and fear of water at age 18: a longitudinal study. *Behav Res Ther*. 1999;37:39-48.
12. Torgersen S. The nature and origin of common phobic fears. *Br J Psychiatry*. 1979;134:343-351.
13. Phillips K, Fulker DW, Rose RJ. Path analysis of seven fear factors in adult twin and sibling pairs and their parents. *Genet Epidemiol*. 1987;4:345-355.
14. Rose RJ, Ditto WB. A developmental-genetic analysis of common fears from early adolescence to early adulthood. *Child Dev*. 1983;54:361-368.
15. Rose RJ, Miller JZ, Pogue-Geile MF, Cardwell GF. Twin-family studies of common fears and phobias. In: Gedda L, Parisi P, Nance WE, eds. *Twin Research 3: Intelligence, Personality, and Development*. New York, NY: Alan R Liss Inc; 1981: 169-174.
16. Neale MC, Fulker DW. A bivariate path analysis of fear data on twins and their parents. *Acta Genet Med Gemellol*. 1984;33:273-286.
17. Kendler KS, Neale MC, Kessler RC, Heath AC, Eaves LJ. The genetic epidemiology of phobias in women: the inter-relationship of agoraphobia, social phobia, situational phobia and simple phobia. *Arch Gen Psychiatry*. 1992;49:273-281.
18. Neale MC, Walters EE, Eaves LJ, Kessler RC, Heath AC, Kendler KS. The genetics of blood-injury fears and phobias: a population-based twin study. *Am J Med Genet*. 1994;54:326-334.
19. Kendler KS, Karkowski LM, Prescott CA. Fears and phobias: reliability and heritability. *Psychol Med*. 1999;29:539-553.
20. Kendler KS, Myers J, Prescott CA, Neale JM. The genetic epidemiology of irrational fears and phobias in men. *Arch Gen Psychiatry*. 2001;58:257-265.
21. Marks IM. *Fears, Phobias, and Rituals*. New York, NY: Oxford University Press; 1987.
22. Eysenck HJ, Eysenck SBG. *Manual of the Eysenck Personality Questionnaire*. London, England: Hodder & Stoughton; 1975.
23. Clark LA, Watson D, Mineka S. Temperament, personality, and the mood and anxiety disorders. *J Abnorm Psychol*. 1994;103:103-116.
24. Kendler KS, Neale MC, Kessler RC, Heath AC, Eaves LJ. A population-based twin study of major depression in women: the impact of varying definitions of illness. *Arch Gen Psychiatry*. 1992;49:257-266.
25. Kendler KS, Prescott CA. Cannabis use, abuse and dependence in a population-based sample of female twins. *Am J Psychiatry*. 1998;155:1016-1022.
26. Kendler KS, Karkowski L, Neale MC, Prescott CA. Illicit psychoactive substance use, heavy use, abuse, and dependence in a US population-based sample of male twins. *Arch Gen Psychiatry*. 2000;57:261-269.
27. Kendler KS, Prescott CA. A population-based twin study of lifetime major depression in men and women. *Arch Gen Psychiatry*. 1999;56:39-44.
28. Robins LN, Helzer JE. *Diagnostic Interview Schedule (DIS): Version III-A*. St Louis, Mo: Washington University School of Medicine; 1985.
29. Kessler RC, Olfson M, Berglund PA. Patterns and predictors of treatment contact after first onset of psychiatric disorders. *Am J Psychiatry*. 1998;155:62-69.
30. Heath AC, Neale MC, Kessler RC, Eaves LJ, Kendler KS. Evidence for genetic influences on personality from self-reports and from informant ratings. *J Pers Soc Psychol*. 1992;63:85-96.
31. Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Meas*. 1960; 20:37-46.
32. Liang K-Y, Scott LZ. Longitudinal data analysis using generalized linear models. *Biometrika*. 1986;73:13-22.
33. SAS Institute. *SAS/STAT Software: Changes and Enhancements Through Release 6.12*. Cary, NC: SAS Institute Inc; 1997.
34. Feild HS, Armenakis AA. On use of multiple tests of significance in psychological research. *Psychol Rep*. 1974;35:427-431.
35. Eaves LJ, Eysenck HJ, Martin NG, Jardine R, Heath AC, Feingold L, Young PA, Kendler KS. *Genes, Culture and Personality: An Empirical Approach*. London, England: Academic Press; 1989.
36. Loehlin JC. *Genes and Environment in Personality Development*. Newbury Park, Calif: Sage Publications; 1992.
37. Poulton R, Waldie KE, Menzies RG, Craske MG, Silva PA. Failure to overcome "innate" fear: a developmental test of the non-associative model of fear acquisition. *Behav Res Ther*. 2001;39:29-43.
38. Roder EL, Timmermans PJ, Vossen JM. Effects of rearing and exposure condition upon the acquisition of phobic behaviour in cynomolgus monkeys. *Behav Res Ther*. 1989;27:221-231.