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Etiology of hypochondriasis: A preliminary behavioral-genetic investigation

Steven Taylor, Gordson JG Asmundson

ABSTRACT

Introduction: Hypochondriasis is a severe mental disorder of unknown etiology. Aims: To investigate the role of genetic and environmental factors in hypochondriasis. Methods: A community sample of 167 pairs of monozygotic twins and 140 pairs of dizygotic twins completed the Illness Attitude Scales. Two empirically validated methods were used to identify cases of hypochondriasis; that is, "caseness" classifications, representing clinically significant (i.e. full or subsyndromal) hypochondriasis. Biometric structural equation modeling was used to investigate the relative importance of additive genetic factors, and shared and nonshared environmental factors. Results: Hypochondriasis was highly heritable; additive genetic factors accounted for 54 to 69% of variance, depending on assessment method. Remaining variance was due to nonshared environment (i.e., environmental factors not shared by members of a given twin pair, such as illnesses experienced only by one member of a given twin pair). Effects of shared environment (factors affecting both twins of a given twin pair) accounted for no variance. Conclusion: To our knowledge, this is the first attempt to estimate the role of genetic and environmental factors for hypochondriasis (defined in terms of caseness). Results highlight the importance of genetic factors. The findings also partially support contemporary cognitive-behavioral models, which emphasize the role of maladaptive learning through environmental experiences. That is, results are consistent with the role of personal illness (e.g., childhood hospitalizations). However, the results do not support the role of parental modeling or parenting styles that lead the child to view oneself as sickly or highly vulnerable to disease (shared environmental factors).

Keywords: Behavioral genetics, Health anxiety, Heritability, Hypochondriasis, Illness Attitude Scales, Twins

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INTRODUCTION

Hypochondriasis is a severe form of health anxiety characterized by preoccupation with fears of having a serious medical condition, based on the misinterpretation of benign somatic symptoms [1]. Preoccupation persists for at least six months, despite

reassurance from medical professionals that the person does not suffer from a serious general medical condition. The disorder is typically chronic and associated with considerable suffering and impairment in social and occupational functioning [1].

The core cognitive feature of hypochondriasis is disease conviction—the belief that bodily sensations and changes are due to serious disease processes rather than benign bodily perturbations, symptoms of minor ailments or autonomic nervous system arousal. Other dysfunctional beliefs (e.g. the belief that one's doctor has not performed all needed tests) may accompany disease conviction and together with disease-related preoccupation and worry, motivate reassurance seeking and recurrent checking behaviors. These maladaptive coping behaviors provide transient relief of distress but, ultimately, serve to perpetuate health anxiety [2–5].

Contemporary models of hypochondriasis are cognitive-behavioral in nature, which emphasize the role of environmental (learning) experiences [2]. These models emphasize the role of parental influences, such as parental modeling of illness behaviors and particular parenting styles (e.g. overprotective parenting) that teach the child to view him or herself as sickly or highly vulnerable to disease. Such models also emphasize the role of early aversive health-related experiences (e.g. childhood hospitalizations) in teaching the person to become fearful of, and catastrophically misinterpret, benign bodily sensations or changes [2].

Although contemporary cognitive-behavioral models have some degree of empirical support [2], they neglect the role of genetic factors. Twin research suggests that health anxiety is influenced by genetic factors [6]. In such research, health anxiety has been assessed dimensionally, ranging from absent to mild to severe. To our knowledge there has been no previously published study on the role of genetic and environmental factors in hypochondriasis, defined in terms of caseness (i.e. clinically significant symptoms, likely reflecting a mix of full and subsyndromal hypochondriasis). The present study of monozygotic (MZ) and dizygotic (DZ) twins is, to our knowledge, the first investigation in this regard.

We sought to determine the relative importance of three types of etiologic factors in hypochondriasis: Additive genetic effects (A), shared environmental factors (C; experiences that are common to both members of a given twin pair, such as parental modeling of illness behavior), and non-shared environmental experiences (E; experiences of one member of a twin pair, such as childhood hospitalization for illness that were not experienced by the co-twin). E also includes measurement error.

MATERIALS AND METHODS

Participants: A community sample of 307 twin pairs (167 MZ, 140 DZ) was recruited from across Canada as part of the University of British Columbia (UBC) twin study. Twins were recruited though newspaper advertisements, print and radio presentations, and twin club registries. Each twin pair was reared together. All participants were fluent in written and spoken English, provided written informed consent, and received an honorarium for completing the study.

The sample consisted of 33 MZ male-male pairs, 134 MZ female-female pairs, 14 DZ male-male pairs, 86 DZ female-female pairs, and 40 DZ male-female pairs. Most were white, 78% were women, and the mean age was 40 years (SD=15 years, range 17 to 81 years). Most (68%) were employed full- or part-time, with the remainder being full-time students (7%), full-time homemakers (7%), retirees (7%), or people subsisting on disability or unemployment benefits (10%).

The sample in this study included the 88 MZ and 65 DZ twin pairs from our previous twin study of health anxiety [6]. In our previous study [6] the sample consisted of 153 twin pairs. For the current study additional twin data were collected, building the sample to a total of 307 twin pairs, which included the original 153 pairs. Our previous study [6] investigated the heritability of health anxiety as defined dimensionally and did not investigate the role of genetic and environmental factors in hypochondriasis as defined as clinically significant symptoms.

Previous research of participants enrolled in the UBC twin study has shown that they are similar to general population samples in terms of symptom and personality variables, and that the assumption of equal environments was supported (i.e. MZ twins are treated no differently from DZ twins by parents, teachers, or others) [7].

Measures: Zygosity was determined by a highly accurate questionnaire [8, 9], along with an examination of recent color photographs. The questionnaire has an accuracy of 93–95% in establishing zygosity, compared with DNA testing [8, 10]. Participants completed a battery of questionnaires including the Illness Attitude Scales (IAS) [11, 12]. The IAS is a 27-item self-report measure designed to assess current fears, beliefs, and attitudes associated with hypochondriasis. Sample items are as follows: "Do you believe that you have a physical disease but doctors have not diagnosed it?", "When you read or hear about an illness, do you get symptoms similar to those of the illness?", "When a doctor tells you that you have no physical disease, do you refuse to believe it?" Items are self-rated on a five point scale (0 - no, 1 - rarely, 2 - sometimes, 3 - often and 4 - most of the time) and can be summed to yield a total score (range - 0–98) or various 3-item subscale scores (range - 0–12) [11, 12]. Two additional items to assess types of treatment and illness experiences are were not used in scoring. Sirri et al. [13] reviewed articles using the IAS published between 1980 to 2006, finding that the measure has excellent discriminant validity (i.e. discriminating between patients with hypochondriasis, patients with other psychiatric conditions, and healthy control participants), excellent concurrent validity (i.e. significant correlations with the other measures of health anxiety), good to very good test-retest reliability

(e.g. subscale rs between .44 and 1.00 on retest evaluations conducted at 1 week to 6 months), and is sensitive to changes with treatment.

Weck et al. [14] recently published IAS cut-off scores that provide an opportunity to estimate the heritability of hypochondriasis defined in terms of clinically significant symptoms (caseness). Those authors developed two IAS cut-off scales, which both performed similarly in terms of their psychometric properties. The first was the total score of the 27-item IAS (IAS-total). A cut-off of 50.5 on the IAS-total was reported as having 95% sensitivity and 90% specificity in diagnosing hypochondriasis, as compared to results from structured clinical interviews. The second was the IAS 3-item Bodily Preoccupation Scale (BPS). Items of the latter are as follows: "When you feel a sensation in your body, do you worry about it?", "When you notice a sensation in your body, do you find it difficult to think of something else?", and "When you read or hear about an illness, do you get similar symptoms?" A cut-off of 5.5 on the BPS was reported as having 92% sensitivity and 90% specificity. Cut-offs from both the BPS and IAS-total were used to define caseness in separate analyses in the present study.

Statistical Methods: Heritability estimates were based on the within-pair similarities of MZ pairs compared to those of DZ pairs. In general, larger within-pair MZ than DZ correlations indicate the presence of genetic effects—that is, effects due to segregating genes—because the greater MZ within-pair similarity is attributed to the twofold greater genetic similarity of MZ than DZ twins. We conducted biometric structural equation modeling, based on robust Weighted Least Squares and within-pair tetrachoric correlations with the program Mx [15]. Modeling involved testing the following models, defined by the genetic factors (A), shared environment factors (C), and nonshared environmental factors (E), proceeding from the least to most parsimonious models: ACE, AE, CE, E. The best-fitting model was the one with the smallest value of Akaike's Information Criterion.

RESULTS

To assess the point prevalence of cases in the present study we randomly labeled, for each twin pair, one individual as Twin 1 (n = 307) and his or her co-twin as Twin 2 (n = 307). For the Twin 1 sample, the cut-offs indicated a hypochondriasis prevalence of 11% (IAS-total) and 13% (BPS). For the Twin 2 sample, the prevalence was 10% and 9%, respectively. These results are higher than the point prevalence of hypochondriasis as assessed by diagnostic measures (<5%) [1], and indicate that the cases likely consisted of a mix of full and subclinical hypochondriasis. Classifications based on the IAS-total versus BPS were significantly related in terms of the people who were or were not classified as cases of hypochondriasis; χ^2 (df = 1) >70.00, p <.001 (91% agreement for each of the Twin 1 and Twin 2 samples).

The tetrachoric within-pair correlations for MZ twins were larger than those of DZ twins, suggesting that genetic factors influenced caseness. The MZ and DZ correlations were as follows: IAS-total rMZ = 0.73, rDZ = -0.13; BPS rMZ = 0.56, rDZ = 0.21. Table 1 shows the goodness-of-fit results for the twin models for each of the IAS-total and BPS scales. The table shows that the AE model had the best fit for both the BPS and IAS-total. Table 2 shows the parameter estimates (proportions of variance for A and E) for the best-fitting models. The results indicate that hypochondriasis is strongly heritable, with additive genetic factors (A) accounting for 54 to 69% of variance depending on the method for identify cases, with the remaining variance explained by nonshared environmental experiences (E). Shared environment (C) did not significantly contribute to variance in the classification of caseness. Even when the full ACE model was computed, the value of C was zero for both scales. The values of C (and 95th % confidence intervals) were as follows: IAS total: C = 0.00 (0.00–0.43); BPS: C = 0.00 (0.00–0.63).

Table 1: Fit indices, as based on Akaike's Information Criterion.

Scale	ACE	AE	CE	E
IAS total	−2.36	−4.36*	1.67	35.07
BPS	−5.91	−7.91*	−6.19	5.73

*Best fitting model.
Abbreviations: IAS - Illness Attitude Scale; BPS - Bodily Preoccupation Scale; A - additive genetic effects; C - shared environmental effects; E - nonshared environmental effects.

Table 2: Proportions of explained variance (and 95th % confidence intervals).

Scale	A	E
IAS total	0.69 (0.47–0.92)	0.32 (0.08–0.53)
BPS	0.54 (0.27–0.83)	0.46 (0.17–0.73)

Abbreviations: IAS - Illness Attitude Scale; BPS - Bodily Preoccupation Scale; A - additive genetic effects; C - shared environmental effects; E - nonshared environmental effects.

DISCUSSION

The results of this preliminary investigation suggest that hypochondriasis, defined broadly to include full-blown and subclinical cases, is strongly influenced by genetic factors. The model comprising additive genetic effects (A) and nonshared environmental effects (E) provided the best fit to the data, suggesting that hypochondriasis is determined primarily by a mix of genetic factors and nonshared environmental influences (i.e., experiences unique to one member of a twin pair)

such as illness or hospitalization. Shared environment, including family factors such as parental modeling or reinforcement of illness behavior, was not a significant contributor to variance in the classification of caseness. These findings fail to support the importance of shared family influences in the development of hypochondriasis, as suggested by contemporary cognitive-behavioral models [2]; however, the findings are in line with cognitive-behavioral postulates regarding the importance of unique illness experiences.

In term of model fitting, the findings of the present study are consistent with our previous findings in which hypochondriasis was defined dimensionally [6]. In that study, four dimensions derived from previous factor analyses were investigated: a) Fear of illness, disease, pain, and death, b) interference in functioning caused by bodily sensations, c) frequency of treatment-seeking, and d) disease conviction. For each dimension, the best fitting model consisted of A and E. The findings of the present study differ from our previous research in that hypochondriasis was strongly heritable when defined in terms of caseness (A = 0.54–0.69) whereas hypochondriasis was not as strongly heritable when defined dimensionally. For the above-mentioned four dimensions, the values of A were, respectively, 0.37, 0.34, 0.13, and 0.10 [6]. In other words, hypochondriasis was most strongly heritable when it was defined as clinically significant symptoms (caseness), compared to when it is defined as separate severity dimensions. Taxometric research has produced equivocal results as to whether hypochondriasis is categorical or dimensional in nature, with some research indicating that it is categorical [16] and other studies indicating that it is dimensional [17, 18]. Further taxometric research is required to resolve this issue. Research is also needed to determine why hypochondriasis is more strongly heritable when defined as a category rather than as a set of dimensions.

The absence of nonshared (e.g. family modeling) environmental effects is not limited to hypochondriasis; similar findings have been reported for other clinical conditions, including twin studies of symptoms of obsessive-compulsive disorder, posttraumatic stress disorder, and panic disorder [19–21]. Further research is needed to investigate whether hypochondriasis is genetically related to other somatoform disorders, to other disorders, such as anxiety disorders, and to broad personality factors such as neuroticism.

Limitations of this study include the lack of a structured diagnostic measure. In the Weck et al. validation study of the IAS scales used in this study [14], hypochondriasis was diagnosed according to structured diagnostic interviews, and the IAS scales were validated against the interview-based diagnosis of hypochondriasis, regardless of whether the participant had a comorbid general medical or psychiatric disorder. The results of the Weck et al. validation study, such as data on sensitivity and specificity, suggests that it is unlikely that caseness, as assessed by the IAS scales, would include a substantial proportion of misclassified participants. Nevertheless, in the present study our reliance on a questionnaire measure is a limitation. Future research is required to determine whether our findings can be replicated with diagnoses of hypochondriasis based on structured clinical interviews.

Another limitation is that nonadditive (dominance or epistatic; genetic effects were not investigated because tests of such effects typically require samples consisting of thousands of twin pairs in order to yield reliable results. In studies of psychopathologic phenomena other than hypochondriasis, nonadditive effects tend to be quite small compared to additive effects, typically accounting for less that 10% of explained variance [19, 22]. If there were nonadditive genetic effects in the present study, they would be subsumed within A, in which A would represent genetic factors broadly defined (additive and nonadditive).

A further limitation is that the classical twin method used in the present study is unable to simultaneously evaluate nonadditive genetic effects and shared environment. Nevertheless, in light of previous research on various forms of psychopathology [19, 22], in which shared environment and nonadditive genetic effects play a minor role, it is likely that the etiology of hypochondriasis is primarily due to a combination of additive genetic effects and nonshared environment. Although the existing research suggests that C and D effects tend to be very small, compared to A and E effects, such results are limited by the fact that the classical twin design does not permit the simultaneous evaluation of C and D. An alternative design, which can simultaneously estimate C and D effects, is to use sibling data in which one of the sibs is adopted [23]. Such a design is difficult to implement because pairs of adopted/nonadopted sib pairs are relatively rare compared to twin pairs.

The nature of the genes underlying hypochondriasis remains to be elucidated. Research suggests that people with hypochondriasis, compared to controls, are no better at detecting bodily sensations (i.e. they do not have superior interoceptive acuity), but they are more likely to report experiencing aversive sensations, such as aches, pains, and palpitations [2]. It is possible that the genetic factors involved in the occurrence of pain or autonomic arousal could also influence a person's degree of hypochondriasis. That is, a person who is genetically predisposed to experience significant pain or autonomic surges may be at heightened risk for acquiring beliefs and fears about the dangerousness of the sensations. If this hypothesis is correct, then hypochondriasis would be the indirect consequence of the genes influencing the tendency to experience aversive bodily sensations. It is also possible that some of the genetic factors in hypochondriasis also influence other forms of psychopathology. A challenge in studying the genetic basis of complex psychiatric disorders such as hypochondriasis is that the disorders are likely to be influenced by multiple genes, with each exerting a small effect on the risk for developing the disorder [24]. In order to detect such small effects, genetic association studies using very large samples are required.

CONCLUSION

To our knowledge, this is the first attempt to estimate the role of genetic and environmental factors for hypochondriasis defined as clinically significant symptoms (caseness). Results highlight the importance of genetic factors. The findings also partially support contemporary cognitive-behavioral models, which emphasize the role of maladaptive learning through environmental experiences. That is, the results are consistent with the role of personal illness (e.g. childhood hospitalizations). However, the result do not support the role of parental modeling or parenting styles that lead the child to view oneself as sickly or highly vulnerable to disease (shared environmental factors).

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Author Contributions

Steven Taylor – Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Critical revision of the article, Final approval of the version to be published

Gordon JG Asmundson – Conception and design, Drafting the article, Critical revision of the article, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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