



LETTER

Genetic and environmental influences on vaccine hesitancy

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1. Introduction

Polarizing attitudes toward the COVID-19 vaccine continue to impede public health efforts to control the spread of the SARS-Cov-2 virus. Approximately 80% of the US population report having been vaccinated at least once, but refusal rates are as high as 30% in some states. Despite the recommendations from the Centers for Disease Control and Prevention (CDC), only 22% of adults have received an updated second dose of the vaccine [1].

The present study was conducted to examine the role of genetic and environmental factors in vaccine hesitancy. Early twin studies of attitudes suggest that both genetic and environmental factors contribute to differences in political and social behavior [2,3]. For example, political affiliation and conservatism, attitudes that have been associated with vaccine resistance, have a significant genetic influence. Social-environmental factors have been strongly implicated in vaccine hesitancy, but the extent to which genetic factors contribute remains uncertain [4]. Given the rising rates of COVID-19 and the emergence of new COVID variants, we utilized a twin design to assess the genetic and environmental influences on vaccine acceptance (and hesitancy).

2. Methods

2.1. Subjects

Between June 2020 and October 2021, information on acute COVID-19 and vaccine acceptance was collected on monozygotic (MZ) and dizygotic (DZ) adult twins, recruited from the Mid-Atlantic Twin Registry (MATR). Twins were eligible to participate if both twins were registered in the MATR and if at least one twin had been seen within the Virginia Commonwealth University (VCU) health system. Self-report data were collected using an online research platform developed by Vibrent (United States of America).

2.2. Assessment

Twins were asked: "Since January 2020, have you been sick for more than 1 day with an illness related to COVID-19 symptoms? Did you receive the COVID-19 vaccine in the past year? If not, when a COVID-19 vaccine is available, how likely are you to want to get the vaccine? If not, what factors make you less likely to get the vaccine?". A validated series of questions on twin similarity was used to classify the twins as MZ or DZ [5]. The study was approved by the VCU Institutional Review Board (IRB) (#HM200021382).

Table 1. Additive genetic, shared environmental, and non-shared environmental components of variance for vaccine hesitancy

Model	Genes	Shared environment	Non-shared environment	$-2 \ln(L)$	Df	χ^2 diff	P
ACE	0.0	0.77	0.23	489.77	3	-	-
E	0.0	0.0	1.00	548.65	5	58.88	<0.0001
CE*	0.0	0.77	0.23	489.77	4	0	ns
AE	0.35	0.0	0.65	495.88	4	6.11	<0.001

Note: *Best-fitting model.

Abbreviations: $-2 \ln(L)$: Goodness of fit; A: Genes; C: Shared environment; E: Non-shared environment; Df: Degrees of freedom; ns: Non-significant; χ^2 diff: Chi-square difference.

2.3. Data analysis

The comparison in similarity of MZ versus DZ twins is the foundation for estimating the contribution of genetic, shared environmental, and non-shared environmental factors to vaccine hesitancy [6]. Additive genetic effects reflect the average effect of individual alleles and genetic loci of a trait. Because MZ twins (on average) share 100% of their genes and DZ twins 50% of their genes in common, a higher MZ correlation to DZ correlation suggests that genetic factors are influencing the trait. Common environmental effects describe influences which make family members more alike compared to random pairs of individuals, such as peers, family, and the wider community. This shared environment is reflected in a DZ correlation greater than one-half the MZ correlation. Unique environmental factors (including error of measurement) are those variables that affect only one MZ twin of the pair and create differences in MZ twins despite their identical genotypes. Tetrachoric correlations for vaccine acceptance in the MZ and DZ twins were estimated using SAS software [7]. Genetic and environmental models, controlling for age and sex, were fitted to the twin data using the statistical program OpenMx [8].

3. Results and Discussion

Female twins, particularly MZ twins, were more highly represented than male twins. The age range of the twins was 18.2 – 72.4 with a median age of 35.1 for the MZ twins and 34.8 for the DZ twins.

Nearly half of the twins (47%) indicated that they had acute COVID-19 symptoms since 2020 ($n = 540$). By October 2021, 90% of the sample indicated that they were vaccinated ($n = 1035$). From a potential sample of 3586 twins, 1793 were successfully contacted via email or phone. Out of these, 1150 individual twins, comprising 325 MZ and 115 DZ twin pairs, provided their data.

Of the 115 twins that were not vaccinated: (i) 60% indicated “a lack of trust” was the reason for not getting the vaccine; (ii) 10–20% said: “It will not help,” “Vaccination is worse than being ill,” “It is just a virus/not fatal/not necessary,” “It depends on the risks/adverse events,” “I am not in a risk group with underlying conditions,” and/or “I need more information first;” and less than 10% said: “I will not get/am never sick,” “I never get vaccinated,” “I do not want to pay for it,” and/or “My region is not a high-risk area.”

The tetrachoric correlations for vaccine acceptance indicate a high degree of similarity in the MZ and DZ twins (0.78 vs. 0.81, respectively), suggesting that genes have little effect on one’s willingness to be vaccinated. Table 1 displays the results of the model fitting, inclusive of alternative models, their goodness of fit

($-2 \ln[L]$), and the Chi-square (χ^2) difference between them. The standardized genetic and environmental components of variance are reported for each model. The full model comprised additive genetic factors (A), shared environmental factors (C), and non-shared environmental factors (E) and was tested against three alternative models: (i) A model with unique environmental factors alone (E); (ii) a model without a genetic influence (only C and E); and (iii) a model without the shared environment (only A and E).

The full three-parameter model provided a good fit to the data ($-2 \ln[L] = 489.77$). Eliminating the genetic parameter (A) did not affect the fit of the model ($-2 \ln[L] = 489.77$; 1 degree of freedom [Df]), whereas eliminating the shared environment (C) resulted in a significantly worse fit ($-2 \ln[L] = 495.88$; χ^2 difference = 6.11; 1 Df; $P < 0.001$). For the best-fitting CE model, 77% of the variation in vaccine hesitancy is accounted for by environmental factors shared by the twins.

4. Conclusion

This study provides strong empirical support for the role of the environment in vaccine acceptance. In contrast to studies of other social–political attitudes, genetic factors do not play a role. The overwhelming information from the media and government agencies about getting vaccinated is the most likely explanation for these findings. A lack of trust was by far the most important reason for vaccine hesitancy. The results underscore the need for bold new strategies to expedite the acceptance of the COVID-19 vaccine and other vaccines that offer protection from viral outbreaks in the future.

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Conflict of Interest

The authors declare no conflicting interest.

Ethics Approval and Consent to Participate

Informed consent was obtained before the subjects participated in the study through the virtual data platform. The study was approved by the VCU IRB (HM200021382).

Consent for Publication

The consent includes the possibility of data sharing. Requests for data are facilitated by the Mid-Atlantic Registry (MATR) according to IRB-approved Data Transfer and User Agreements.

Availability of Data

Data are available from the corresponding author on reasonable request.

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