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Depression and Genetic Causal Attribution of Epilepsy in Multiplex Epilepsy Families

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Summary

Objectives—Rapid advances in genetic research and increased use of genetic testing have increased the emphasis on genetic causes of epilepsy in patient encounters. Research in other disorders suggests that genetic causal attributions can influence patients' psychological responses and coping strategies, but little is currently known about how epilepsy patients and their relatives will respond to genetic attributions of epilepsy. We investigated the possibility that depression, the most frequent psychiatric comorbidity in the epilepsies, might be related to the perception that epilepsy has a genetic cause among members of families containing multiple individuals with epilepsy.

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Supplemental Materials. Analyses to Assess Potential Confounding

Disclosures

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Methods—A self-administered survey was completed by 417 individuals in 104 families averaging four individuals with epilepsy per family. Current depression was measured with the PHQ-9. Genetic causal attribution was assessed by three questions addressing: perceived likelihood of having an epilepsy-related mutation, perceived role of genetics in causing epilepsy in the family, and (in individuals with epilepsy) perceived influence of genetics in causing the individual's epilepsy. Relatives without epilepsy were asked about their perceived chance of developing epilepsy in the future, compared with the average person.

Results—Prevalence of current depression was 14.8% in 182 individuals with epilepsy, 6.5% in 184 biological relatives without epilepsy, and 3.9% in 51 married-in individuals. Among individuals with epilepsy, depression was unrelated to genetic attribution. Among biological relatives without epilepsy, however, prevalence of depression increased with increasing perceived chance of having an epilepsy-related mutation (p=0.02). This association was not mediated by perceived future epilepsy risk among relatives without epilepsy.

Significance—Depression is associated with perceived likelihood of carrying an epilepsy-related mutation among individuals without epilepsy in families containing multiple affected individuals. This association should be considered when addressing mental health issues in such families.

Keywords

epilepsy; epidemiology; genetics; depression; genetic attribution

Introduction

Genetic research in the epilepsies is advancing rapidly, holding promise for the development of new precision medicine approaches to improve clinical management for some patients.[1] Genetic testing is increasingly being incorporated into clinical care,[2] and researchers and clinicians are now strongly emphasizing the importance of genetics in the cause of epilepsy.[3] Little is currently known about how people with epilepsy and their family members will react to this emphasis on genetic causes. For some individuals, genetic causal attribution may bring relief that a cause is identified and optimism for development of improved treatments, whereas for others, responses may be more complex.[4]

The ways in which people conceptualize the causes of their health conditions can have an important influence on their treatment-seeking behavior, psychological responses, and coping strategies.[5] Previous research suggests that "stable" and "uncontrollable" causal attributions, including heredity, may be associated with negative psychological adjustment strategies.[6] In research on mental illness, genetic and biological causal attributions have been found to be associated with "prognostic pessimism" among affected individuals.[7] Similarly, some mental illnesses are viewed by the general public as more serious and less treatable when they are perceived to have a genetic cause.[8,9] However, the impacts of genetic causal attributions may vary among different disorders. A qualitative study of individuals with four conditions (deafness/hearing loss, breast cancer, sickle cell disease, and cystic fibrosis) found that genetic attributions had both negative and positive psychosocial impacts that were shaped by the context of the lived experience of each condition.[10] Among patients with "unexplained physical symptoms," comorbidity with depression and anxiety was

associated with more psychological, as opposed to genetic, attributions.[11] For obesity, findings regarding the impact of genetic causal attributions have varied, with some studies showing no effect,[12–14] and others showing an association of genetic attributions with reduced control over eating.[15,16]

In this paper, we investigated the relations of depression, the most frequent psychiatric comorbidity in the epilepsies,[17,18] to the perception that epilepsy has a genetic cause. The data are from a survey of families containing multiple individuals with epilepsy who previously participated in genetic research. Our earlier findings from this study show that interest in genetic testing is strong in these families, particularly when it is likely to lead to improved clinical care.[19,20] We also found that felt stigma was increased in family members with epilepsy who perceived genetics played a “medium” or “big” role in causing epilepsy in the family.[21]

Comorbidity of epilepsy with depression could arise from multiple mechanisms, including psychosocial impacts of having epilepsy, effects of antiepileptic treatments, and shared pathophysiologic mechanisms possibly mediated by shared genetic susceptibility.[18,22] Only a few studies have examined prevalence and predictors of depression in families containing multiple individuals with epilepsy.[23,24] Study of depression in such families offers an opportunity to address both shared genetic mechanisms and psychosocial impacts. However, our primary interest in the current study was on psychosocial impacts, particularly focused on the hypothesis that genetic attribution would be associated with increased prevalence of current depression.

Methods

Participants

The study sample comprised individuals who participated in the Epilepsy Family Study of Columbia University (EFSCU), a long-term investigation that began in the 1980’s as a familial aggregation study and evolved into a genetic linkage study.[25] Eligibility for the linkage study required that each family contain either a sibling pair or three or more individuals with epilepsy of unknown cause, regardless of syndrome. Recruitment was carried out throughout the United States, by soliciting physician referrals and self-referrals in response to advertisements through the Epilepsy Foundation and a study web site. Participants were enrolled from 1993–2007, and have been re-contacted periodically through newsletters and invitations to participate in additional studies. They have been followed for a mean of 14 (range 6–21) years; and 85% for more than 10 years.

Individuals were eligible for the current study if they previously participated in the genetic research by being interviewed or donating a blood sample, and were currently aged 18–79 years, able to complete a self-administered survey in English, and willing to be contacted for future research. After excluding those who did not meet these criteria, 929 individuals in 113 families were eligible, including 330 who had a history of epilepsy based on our previous investigations, 441 biological relatives without epilepsy, and 158 who were married-in to the families.

Eligible individuals were asked to complete a self-administered questionnaire of approximately 30-minutes, either online through Survey Monkey (www.surveymonkey.com) or on paper. They were offered $20 in compensation for their participation. The Columbia University Medical Center Institutional Review Board approved the research protocols for the study.

Epilepsy History

Individuals were classified as having epilepsy if they responded "yes" to either of two survey questions. The first question asked "Which of your biological relatives have had epilepsy or a seizure disorder?" followed by a list of relative types with "Yourself" at the top. The second question, included in a later section of the survey that addressed respondents' seizure histories in more detail, asked "Have you ever been told that you had epilepsy or a seizure disorder?" We used self-reported data rather than diagnoses from our original genetic study (based on epileptologist review of data from semistructured interviews and medical records),[25] because an individual's perception of whether he or she had epilepsy may be most relevant for assessment of associations of current depression with genetic attribution, and in most cases, a long time period had elapsed since our previous assessment. Self-reports agreed with our previous diagnoses of epilepsy in most participants (kappa=0.87, or "almost perfect" agreement according to Landis and Koch[26]). Eight participants reported onset of epilepsy after our last contact with them.

Depression

To screen for current depression, we used the mood subscale of the Patient Health Questionnaire (PHQ-9), with a positive screen defined by a score ≥ 10.[27,28] A recent study validated use of this score for individuals with epilepsy.[29]

Genetic Causal Attribution

We used three questions to measure genetic causal attribution of epilepsy (Table 1). These questions asked participants to evaluate (1) the chance they had a "change or mutation in a gene that affects risk for epilepsy," (2) the role of genetics in causing epilepsy in their family, and (3) (for individuals with epilepsy only) the role of "genetics or inheritance" in causing their epilepsy. In relatives without epilepsy, we also asked a question about the perceived risk of developing epilepsy in the future, compared with the average person (Table 1).

Statistical Analysis

For analysis, we estimated prevalence ratios (PRs) through Poisson regression models with robust standard errors,[30] using generalized estimating equation (GEE) models to account for non-independence resulting from inclusion of multiple individuals per family. We first compared prevalence of current depression among the major subgroups: participants with epilepsy, biological relatives without epilepsy, married-in individuals. Then we assessed associations of current depression with genetic attribution measures, separately in individuals with epilepsy and biological relatives without epilepsy. To test the hypothesis

that prevalence of depression increased with rising levels of genetic attribution, we used models in which the genetic attribution measures were treated as linear covariates.

We evaluated the potential confounding effects of demographic variables (age, sex, education, and employment), number of relatives with epilepsy reported in the survey, epilepsy severity measures (total lifetime seizures: ≤ 20, 21–100, >100; and time since last seizure: ≤ 5 years, >5 years), and perceived future epilepsy risk in biological relatives without epilepsy (Supplemental Materials). For these analyses, we assessed the association of each potential confounder with current depression (outcome), genetic attribution measures (exposures), and major subgroup ("exposure" for comparisons among subgroups). We adjusted for variables that were not theorized to be in the causal pathway and were associated with both the outcome and the exposure, using a threshold of p=0.20. Analyses were conducted with IBM SPSS Statistics for Windows, Version 22.0 (IBM Corporation, Armonk, NY, U.S.A.).

Results

Between January 11, 2013 and May 8, 2015, we reached 701 (76%) of the 929 eligible individuals by telephone to invite participation; 592 (85%) of those reached agreed to participate; and 431 (73%) of those who agreed completed the survey, giving an overall participation rate of 46%. The 431 individuals who completed the survey were members of 104 families with an average of four (range 1–24) participants per family and an average of four (range 2–17) individuals with epilepsy per family based on our previous assessments.

As reported previously,[20] survey participation rates increased with advancing age, and were higher in women than in men, in college graduates vs. non-graduates, and in individuals with epilepsy, compared with biological relatives without epilepsy or married-in individuals. Individuals who completed the survey averaged 53 years of age (SEM 0.70), and 88% were white, non-Hispanic, 59% women, and 54% college graduates. We excluded individuals who had missing data on the PHQ-9 (N=14), resulting in a final sample of 417 individuals.

Comparison of major subgroups

Prevalence of current depression was 14.8% in individuals with epilepsy and 6.5% in biological relatives without epilepsy (age-adjusted PR=2.3, 95% confidence interval [CI] 1.11–4.65, p=0.02). Prevalence was lower in married-in individuals (3.9%) than in biological relatives without epilepsy, but the difference was not significant (age-adjusted PR=0.7, 95% CI 0.19–2.56, p=0.50).

Psychometric properties of genetic attribution measures

We evaluated the psychometric properties of survey items used to assess genetic attribution, since there are no commonly accepted measures of this construct. Cronbach's alpha was 0.77 for the three questions used in individuals with epilepsy and 0.65 for the two questions used in relatives without epilepsy, indicating good reliability. In the absence of a clear gold standard, we assessed concurrent validity by examining associations of responses to the genetic attribution questions with responses to two other survey questions expected to be related to the genetic attribution construct: number of relatives with epilepsy (<4 vs. ≥4), and

perceived future epilepsy risk compared with the average person (more/much more vs. same/less) (Table 2). For all genetic attribution measures, in both individuals with epilepsy and biological relatives without epilepsy, the proportion of participants with ≥4 affected relatives increased with increasing levels of genetic attribution (Table 2). Similarly, unaffected family members with higher levels of genetic attribution were significantly more likely than others to respond that they had future epilepsy risk "more/much more than the average person" (Table 2).

Associations of depression with genetic attribution measures

Among participants with epilepsy, prevalence of current depression was not associated with any of the genetic attribution measures (Table 3). Among biological relatives without epilepsy, however, depression was significantly associated with perceived chance of having an epilepsy-related mutation (Table 4). None of the biological relatives without epilepsy who responded their chance of having an epilepsy-related mutation was "none/small" met criteria for depression; hence PRs could not be computed for this measure. However, in analyses treating perceived chance of having a mutation as a linear covariate, the unadjusted PR was 2.9, reflecting a significant, three-fold increase in the prevalence of depression with each increase in level of genetic attribution. Similarly, the unadjusted PR for the role of genetics in causing in epilepsy in the family, treated as a linear covariate, was 1.8 (p=0.10). Prevalence of depression was also higher in individuals who responded that their future epilepsy risk was "more/much more than the average person" than in others (PR=2.5, p=0.10).

Given the strong associations of both measures of genetic attribution with perceived future epilepsy risk (Table 2), we evaluated the independent effects of these variables on depression by including all of them in the adjusted model along with age. The PR for perceived chance of having a mutation declined to 1.9 but remained significant (p=0.02), while the PR for perceived future epilepsy risk declined to 1.3. The results were essentially unchanged for perceived role of genetics in causing epilepsy in the family.

Finally, because perceived future epilepsy risk is expected to be strongly related to age, we explored whether the association of depression with perceived chance of having a mutation also varied by age. As expected, the proportion of relatives who responded that their future risk was "more/much more than the average person" declined with advancing age (<40 years: 44%, 40–59 years: 32%, ≥60 years: 26%). However, although numbers were too small to draw firm conclusions, there was no evidence that the association of depression with perceived chance of having a mutation was stronger in younger individuals, or that it was restricted to individuals with high perceived future epilepsy risk in any age group.

Discussion

We assessed whether genetic causal attribution of epilepsy was related to current depression in a unique set of families containing multiple individuals with epilepsy. This question has not been investigated before, and is particularly salient because genetic influences on epilepsy are increasingly being emphasized in clinical care, and depression is a significant comorbidity. Our results confirm the well-known association of epilepsy with depression:

current depression was more than twice as prevalent in individuals with epilepsy as in their relatives without epilepsy. They also suggest that beliefs about epilepsy genetics are interconnected with symptoms of depression in family members of individuals with epilepsy.

Since there are no commonly accepted measures of the genetic attribution construct, we assessed the psychometric properties of our questions and found they had good reliability and concurrent validity. All of the questions were strongly associated with two variables reasonably expected to be related to genetic attribution, i.e., number of affected relatives and perceived future epilepsy risk.

Among individuals with epilepsy, we found no significant relationship between genetic attribution and current depression. Among biological relatives without epilepsy, however, current depression was significantly associated with individuals' perception that they are likely to have an epilepsy-related mutation, and marginally associated with their perceived role of genetics in causing epilepsy in the family. Prevalence of current depression was also higher in unaffected family members who responded their future epilepsy risk was "more/much more than the average person" (10.6%) than in others (4.3%). Given this finding, we considered the possibility that the association of depression with genetic attribution was mediated by the perception of high future epilepsy risk. However, our findings are inconsistent with this possibility, because the PR for perceived future epilepsy risk declined to 1.3 (from 2.5) after adjustment for the genetic attribution variables, which would not be expected under a model of mediation. The decline in the PR suggests that the increased prevalence of depression among individuals with high perceived future epilepsy risk was due largely to confounding with genetic attribution.

Because our study is cross-sectional, we cannot draw strong conclusions about the causal direction of the association between depression and perceived chance of having a mutation in unaffected relatives. At least two explanations are possible. First, in some individuals, an individual's belief that he or she is likely to have a mutation may cause depression. We believe our data argue against this interpretation: the strong relationship of genetic attribution with number of relatives with epilepsy (Table 2) likely reflects a causal effect, i.e., having ≥4 affected relatives *leads to* a higher level of genetic attribution. Given this causal relationship, if genetic attribution also *led to* depression, we would expect to observe increased prevalence of depression among individuals with ≥4 affected relatives. However, among relatives without epilepsy, prevalence of current depression was virtually identical in those who reported ≥4 vs. <4 affected family members (6.2% vs. 6.4%, Supplemental Materials, Table 1).

Alternatively, genetic attribution may be a *consequence*, rather than a cause, of depression among unaffected family members. Family members who are depressed may tend to believe they are likely to carry an epilepsy-related mutation in these families. Symptoms of depression, including a sense of powerlessness and doom, might lead some individuals to believe they are likely to carry a mutation. The word "mutation" has been shown to have negative connotations,[31] and this might explain in part why current depression was significantly associated with our question regarding perceived likelihood of carrying a

mutation and not with our question on perceived role of genetics in causing epilepsy in the family. Use of alternative wording may be important for learning about how people with epilepsy and their family members think about genetic causes.

Since these families contain multiple individuals with epilepsy, they are likely to be enriched for genetic influences on epilepsy. Hence, under a hypothesis of shared genetic susceptibility to epilepsy and depression, we would expect an increased prevalence of depression both in individuals with and without epilepsy in these families, which we did not observe. Although comparison with other studies is difficult because of differences in the measures of depression used and the characteristics of epilepsy in the included individuals, the 14.8% prevalence of current depression we observed in individuals with epilepsy is not higher than in other studies of epilepsy.[17] The 6.5% prevalence of current depression in biological relatives without epilepsy is also not higher than findings in the general population.[32–34] Moreover, the lack of association of depression with participants' reports of number of relatives with epilepsy appears to be inconsistent with a hypothesis of shared genetic susceptibility. However, comparison of survey data with findings from our previous genetic studies shows that respondents underreported epilepsy in their families. Also, the PHQ-9 is not very informative for testing a hypothesis of shared genetic susceptibility because it is limited to depressive symptoms in the last two weeks, and is a screen rather than a full diagnostic instrument. To test genetic hypotheses, assessment of lifetime prevalence of depression with a more comprehensive diagnostic instrument would be preferable, and studies are ongoing in our group to do this in a subset of the families included here.

Our study has several limitations. The relatively small sample size hinders our ability to draw strong conclusions. Generalizability is limited by the characteristics of the sample, which consists of unusual families containing multiple individuals with epilepsy who previously participated in genetic research. Members of these families are likely to have higher levels of genetic attribution and knowledge than unselected individuals with epilepsy, although this sample may be especially appropriate for asking questions about the impact of genetic attribution on depression in epilepsy. Another limitation is the selected demographic composition of the sample (88% non-Hispanic whites and 54% college graduates), resulting from self-selection into the original study and participation bias in the current survey, which could have led to reduced levels of depression compared with the general population. Finally, the current analysis examined psychosocial correlates of genetic attribution but did not examine responses to receiving actual genetic test results. Evaluation of responses to receipt of genetic test results is ongoing in our study.

Despite these limitations, our findings suggest that genetic attribution – in particular, the perceived likelihood of carrying an epilepsy-related mutation – is associated with depression in unaffected members of families likely to have a genetic susceptibility to epilepsy. The findings provide evidence for a role of psychosocial factors (as opposed to antiepileptic treatments or shared pathophysiological mechanisms) in explaining the well-established comorbidity of epilepsy and depression. Further research is needed to clarify the reasons for this association, in order to help improve mental health outcomes in families with epilepsy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key points

- In families with multiple affected individuals, prevalence of depression was 14.8% in people with epilepsy and 6.5% in their relatives without epilepsy.
- Among people with epilepsy, prevalence of depression was not associated with the belief that their epilepsy had a genetic cause.
- Among relatives without epilepsy, prevalence of depression was associated with perceived chance of having an epilepsy-related mutation.
- The association of depression with perceived chance of having a mutation was not due to high perceived future epilepsy risk in unaffected relatives.

Table 1

Survey questions relating to genetic attribution and future epilepsy risk

Variable Name	Question wording	Response options[a]
Perceived chance of having an epilepsy-related mutation	In your opinion, what do you think the chances are that you have a change or mutation in a gene that affects risk for epilepsy?	• No chance • Small chance • Moderate chance • High chance • Don't know
Perceived role of genetics in causing epilepsy in family	In your opinion, how big a role has genetics had in causing the epilepsy in your family?	• No role • Small role • Medium role • Big role
Influence of genetics in causing your epilepsy *(people with epilepsy only)*	How much do you think each of the following influenced your risk of developing epilepsy? (Please answer what you think caused your epilepsy in the first place, rather than what you think might trigger your seizures.)[b]	• No influence • Some influence • Strong influence
Perceived future epilepsy risk *(people without epilepsy only)*	In your opinion, would you say your chances of getting epilepsy in the future are…	• Much more than the average person • More than the average person • Same as the average person • Less than the average person • Much less than the average person • Not applicable – I have epilepsy • Don't know

[a] For analysis, responses were divided into three categories for "perceived chance of having an epilepsy-related mutation" (high, moderate, no/small) and "perceived role of genetics in causing epilepsy in family" (big, medium, no/small), and dichotomized for "perceived future epilepsy risk" (much more/more vs. same/less/much less). "Don't know" and "not applicable" responses were excluded.

[b] Factors of possible influence appeared in the following order: head injury, infection of the brain or nervous system, genetics or inheritance, stroke, brain tumor, cerebral palsy, problems during birth or birth injury, fever, exposure to environmental toxins or poisoning, alcohol or drug use, god's will, high stress level, poor diet or exercise, metabolic disorder, other.

Table 2

Association of genetic attribution measures with total affected family members and perceived future epilepsy risk

	Participants with epilepsy:			Biological relatives without epilepsy:					
	Total affected family members			Total affected family members			Perceived future epilepsy risk, compared with average person		
Predictors	**N**	**%≥4**	**PR (95% CI)**	**N**	**%≥4**	**PR (95% CI)**	**N**	**% More/much more**	**PR (95% CI)**
Perceived chance of having an epilepsy-related mutation									
High	62	69.4	3.3 (1.35–8.06)	26	73.1	2.1 (1.34–3.32)	25	72.0	5.6 (2.59–12.29)
Moderate	34	32.4	1.5 (0.57–4.17)	41	41.5	1.2 (0.72–1.99)	36	33.3	2.6 (1.17–5.82)
No/small	19	21.1	1.0 (reference)	52	34.6	1.0 (reference)	47	12.8	1.0 (reference)
p-value			**<0.001**			**0.002**			**<0.001**
Perceived role of genetics in causing epilepsy in the family									
Big	93	68.8	13.8 (3.58–52.93)	69	52.2	3.4 (1.66–6.94)	61	39.3	3.0 (1.26–7.08)
Medium	40	42.5	8.5 (2.16–33.41)	50	42.0	2.7 (1.21–6.17)	38	47.4	3.6 (1.59–8.14)
No/small	40	5.0	1.0 (reference)	52	15.4	1.0 (reference)	38	13.2	1.0 (reference)
p-value			**<0.001**			**0.002**			**0.007**
Perceived role of genetics in causing your epilepsy									
Strong	95	62.1	5.3 (1.56–17.91)						
Some	44	36.4	3.1 (0.84–11.38)						
None	17	11.8	1.0 (reference)						
p-value			**0.001**						

PR, prevalence ratio, CI, confidence interval, computed from GEE model.

Table 3

Participants with epilepsy: Relations of depression to genetic attribution measures

			Unadjusted		Adjusted[a]	
Predictors	**N**	**% depressed**	**PR (95% CI)**	**p-value**	**PR (95% CI)**	**p-value**
Perceived chance of having an epilepsy-related mutation						
High	62	14.5	1.1 (0.32–3.56)	0.92	1.7 (0.23–13.32)	0.59
Moderate	37	24.3	1.8 (0.55–5.77)	0.33	2.6 (0.33–20.76)	0.37
No/small	22	13.6	1.0 (reference)	(ref.)	1.0 (reference)	(ref.)
Predictor treated as linear covariate	121		0.9 (0.59–1.45)	0.74	1.0 (0.57–1.81)	0.96
Perceived role of genetics in causing epilepsy in family						
Big	93	14.0	1.4 (0.48–4.09)	0.54	1.2 (0.39–3.98)	0.72
Medium	45	17.8	1.8 (0.59–5.40)	0.31	1.6 (0.40–6.13)	0.51
No/small	40	10.0	1.0 (reference)	(ref.)	1.0 (reference)	(ref.)
Predictor treated as linear covariate	178		1.1 (0.71–1.72)	0.67	1.0 (0.60–1.65)	0.99
Influence of genetics in causing your epilepsy						
Strong	98	17.3	1.6 (0.44–6.15)	0.46	1.1 (0.39–3.36)	0.81
Some	45	13.3	1.3 (0.29–5.51)	0.75	0.8 (0.20–3.13)	0.75
None	19	10.5	1.0 (reference)	(ref.)	1.0 (reference)	(ref.)
Predictor treated as linear covariate	162		1.3 (0.73–2.27)	0.38	1.2 (0.66–2.10)	0.57

PR, prevalence ratio, CI, confidence interval, computed from GEE model.

[a]Adjusted for sex, education (college graduate vs. others), total lifetime seizures (≤20, 21–100, >100 and time since last seizure (≤5 years, >5 years).

Table 4

Biological relatives without epilepsy: Relations of depression to genetic attribution measures and perceived future epilepsy risk

			Unadjusted		Adjusted[a]	
Predictors	**N**	**% depressed**	**PR (95% CI)**	**p-value**	**PR (95% CI)**	**p-value**
Perceived chance of having an epilepsy-related mutation						
High	27	14.8	N/A	N/A	N/A	N/A
Moderate	41	12.2	N/A	N/A	N/A	N/A
No/small	53	0.0	N/A	N/A	N/A	N/A
Predictor treated as linear covariate	121		2.9 (1.60–5.42)	0.001	1.9 (1.12–3.39)	0.02
Perceived role of genetics in causing epilepsy in family						
Big	73	9.6	4.9 (0.59–40.64)	0.142	N/A	N/A
Medium	51	7.8	4.0 (0.67–24.01)	0.129	N/A	N/A
No/small	51	2.0	1.0 (reference)	(ref.)	N/A	N/A
Predictor treated as linear covariate	175		1.8 (0.90–3.77)	0.10	2.0 (0.82–4.66)	0.13
Perceived future epilepsy risk, compared with average person						
More/much more	47	10.6	2.5 (0.83–7.37)	0.10	1.3 (0.30–5.24)	0.76
Same or less	93	4.3	1.0 (reference)	(ref.)	1.0 (reference)	(ref.)

PR, prevalence ratio, CI, confidence interval, computed from GEE model.

[a]Adjusted for age and all variables in table.