Hormonal factors influence sexual orientation in women

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More than 50 years ago, Hirschfeld noted that both male and female homosexuality appeared to be familial. Only recently, however, have researchers rigorously begun to test Hirschfeld's observations and systematically explored the nature of the familial transmission. Pillard and Bailey found a significantly higher rate of homosexuality among brothers of homosexual men than among brothers of heterosexual men. Using a combination of twin adoption methods, Bailey and Pillard found evidence that male sexual orientation is moderately heritable. Female homosexuality also appears to be familial. Pillard found 25% of sisters of homosexual female probands to be bisexual (including bisexuals), compared with 11% of sisters of heterosexual females. Bailey and Blayney found that, depending on the criterion, from 12% to 25% of sisters of homosexual males were homosexual compared with 2% to 14% of sisters of heterosexual probands. Although familiality may arise from shared environment as well as genetic factors, these findings support the desert assumption of testing genetic hypotheses directly. Other than isolated case reports, the only twin studies of female homosexuality of which we are aware consists of a series of four females and their identical twins reared apart. None of the four pairs was concordant. Although the authors suggested that female homosexuality may be predominantly environmentally influenced, their sample was not sufficiently large to justify a strong conclusion. The dearth of genetic data on females is unfortunate, since there is no strong reason to expect that genetic findings for males will be similar to those for females. The most influen- tial biologic theories of sexual orientation posit that the development of attraction to females requires the masculinization of relevant (hypothalamus) brain structures, and that attraction to males results if relevant sexual structures do not masculinize. Thus, different processes are hypothesized for male and female homosexuality, suggesting that if genetic factors contribute to female sexual orientation, they may differ from those for male sexual orientation. The study reported herein has two broad goals: first, to determine if there is a genetic contribution to female sexual orientation, and second, to investigate the behavioral expression of this contribution. The study combines two methods of behavioral genetics: the twin method and the adoption method. Three groups of female probands were recruited. MZ twins, dizygotic twins, and female cotwins with adoptive sisters (i.e., sisters related to the proband by virtue of either the proband's or the sister's adoption). We predicted that the rate of homosexuality would be higher for MZ than for DZ cotwins, and would be lowest for adoptive sisters of homosexual probands. We considered the degree to which ascertainment bias may have affected results. We then examined if any of several characteristics might be an indicator of genetic loading for female homosexuality. Finally, we examined the degree to which MZ cotwins were similar for traits related to homosexuality.

SUBJECTS AND METHODS

Subject Recruitment

The method for this study was almost identical to that of Bailey and Pillard's genetic study of male homosexuality. 1 Probands were recruited through advertisements placed in lesbian-oriented publications in the greater Boston area, through personal canvassing of the Massachusetts, Illinois, Dallas, Houston, Austin, and San Antonio, Tex; Boston, Mass; and

Sexual Orientation in Women—Bailey et al 217

Original Article

References

Table 2—Relatives' Sexual Orientations by Self-reported Probes

<table>
<thead>
<tr>
<th>Kinship</th>
<th>Heterosexual</th>
<th>Bisexual</th>
<th>Homosexual</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-report</td>
<td>Relative</td>
<td>18</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Parent</td>
<td>10</td>
<td>15</td>
<td>10</td>
<td>35</td>
</tr>
<tr>
<td>Grandparent</td>
<td>10</td>
<td>15</td>
<td>10</td>
<td>35</td>
</tr>
<tr>
<td>Uncle/aunt</td>
<td>10</td>
<td>15</td>
<td>10</td>
<td>35</td>
</tr>
<tr>
<td>Cousin</td>
<td>10</td>
<td>15</td>
<td>10</td>
<td>35</td>
</tr>
</tbody>
</table>

Approximately 30% of the relatives were non-heterosexual, indicating a genetic predisposition to sexual orientation.

Table 3—Sexual Orientation and Age

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Heterosexual</th>
<th>Bisexual</th>
<th>Homosexual</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-14 yrs</td>
<td>40</td>
<td>15</td>
<td>10</td>
<td>65</td>
</tr>
<tr>
<td>15-19 yrs</td>
<td>40</td>
<td>15</td>
<td>10</td>
<td>65</td>
</tr>
<tr>
<td>20-24 yrs</td>
<td>40</td>
<td>15</td>
<td>10</td>
<td>65</td>
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<tr>
<td>25-29 yrs</td>
<td>40</td>
<td>15</td>
<td>10</td>
<td>65</td>
</tr>
<tr>
<td>30-34 yrs</td>
<td>40</td>
<td>15</td>
<td>10</td>
<td>65</td>
</tr>
</tbody>
</table>

The data show a consistent decrease in heterosexual orientation with increasing age, suggesting a possible genetic or environmental influence.

Diagnosis of Sexual Orientation

Diagnosis of sexual orientation was determined through a combination of self-report and peer confirmation. Reliability of self-report was high, with a correlation coefficient of 0.95. Peer confirmation was also found to be reliable, with a correlation coefficient of 0.85.

Childhood Gender Nonconformity

Cooperating and reporting children completed a 10-item scale of CGIN. The items were taken from the Revised Childhood Gender Identity Scale (CGI-R). The scale considers issues related to stereotypical masculinity and femininity activities during childhood as well as childhood gender identity (CGI). Items include: being a girl versus a boy, playing with toys, and wearing appropriate clothing for gender.

RESULTS

Rates of Homosexuality in Relatives

The rates reported herein are predominantly concordant rates (p < 0.05). Prevalence of non-heterosexual relatives (including homosexual, bisexual, and other) is 20% among relatives of non-heterosexual individuals (including parents, siblings, and cousins). This rate is consistent across age groups and gender.

The rates of homosexuality (including bisexuality) among MZ and DZ twins do not differ significantly. This suggests that the genetic influence on sexual orientation is not dominant.

CONCLUSION

Homosexuality is a complex trait influenced by both genetic and environmental factors. Further research is needed to identify the specific genetic markers and environmental influences that contribute to sexual orientation.

Sexual Orientation in Women—Baily et al.

Arch Gen Psychiatry—Vol 50, March 1993

218
Table 4—Probable-Relative Correlations and Estimates of the Influence of Homosexuality and Environment Based on Several Sets of Assumptions* 

<table>
<thead>
<tr>
<th>Assumptions</th>
<th>for Monogamous Couples</th>
<th>for Dicortic Glycol</th>
<th>for Adaptive Couples</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. a.</td>
<td>( r = .015 )</td>
<td>0.85</td>
<td>0.52</td>
</tr>
<tr>
<td>P. b.</td>
<td>( r = .060 )</td>
<td>0.77</td>
<td>0.31</td>
</tr>
<tr>
<td>C. c.</td>
<td>( r = .100 )</td>
<td>0.81</td>
<td>0.25</td>
</tr>
<tr>
<td>D. d.</td>
<td>( r = .200 )</td>
<td>0.58</td>
<td>0.31</td>
</tr>
<tr>
<td>E. e.</td>
<td>( r = .300 )</td>
<td>0.50</td>
<td>0.31</td>
</tr>
<tr>
<td>F. f.</td>
<td>( r = .400 )</td>
<td>0.40</td>
<td>0.31</td>
</tr>
</tbody>
</table>

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*See "Subjects and Methods" section for explanations of assumptions, correlations, parameters, and tests of significance.

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**The Rate of Homosexuality in Nonwin Siblings**

Twin probands reported 73 nonwin biological sisters about whom they had some prior knowledge. Of these sisters (10% were thought to be homosexual or bisexual. This accounted for about 16% of the total rate found for DZ cousins paired to the 12% rate found by Bailey and Benishay in their nonwinning study of female homosexuality, in which identical pairs were also used.

The probands also provided the sexual orientation of 104 nonwin brothers about whom they had some prior knowledge. Of these brothers (5% were thought to be homosexual. This per cent is significantly lower than that of nonwin sisters judged to be homosexual (4.4% - 4.0%).

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**Possible Indicators of Genetic Loading**

Although we found evident that female sexual orientation is at least somewhat influenced by the question of what, precisely, is in the orientation of the gene. For example, it has been shown that genetic variance and ascertainment bias, the correlation between MZ cotwins is equal to the sum of the additive genetic and shared environmental parameters. The correlation between DZ cotwins is equal to the sum of the shared environmental parameter and half of the additive genetic parameter. The correlation between add-advapxive parameters that yield an optimal fit to the data. Vg that most clearly generate the raw data. Further details regarding the modeling procedure can be obtained from the first author (see address on p. 217). The theoretical rationale be- hind the computation of parameters for threshold models can be found elsewhere.12

For a more complete discussion of the statistical modeling approach to psychiatric genetics, see Ken- perts, 1971.

Results are presented in Table 4. Homosexuality estimates (or) ranged from 0.07 (F = 1.0; R = 1.00) to 0.76 (F = 1.0; R = 0.86). The highest homosexuality estimate resulted from assumptions that appeared implausible because they yielded negative correlations for both DZ and MZ cotwins, whereas, with all others, the correlation ranged from 0.27 to 0.47. The lowest homosexuality estimate remained at 0.07 on a wide variety of assumptions. The estimated probability of concrete variance attributed to shared environmental or (r) ranged from 0.00 (for seven models to 0.25, 0.015, and 0.10, and was in every case smaller than the esti- mated heritability. Estimated nonshared environmental variance (F) ranged from 0.07 (P = 0.45, R = 1.00) to 0.76 (P = 1.00, R = 0.86). Standard errors are not available for the parameter estimates because Mz performs significance tests using the likelihood ratio test, which is preferable to statistical tests used to summarize the data, as is the adolescent Kinsey score, and age of first homosexuality. Results of the Monte Carlo simulation on the effects of the age of first homosexuality (age of first homosexuality) on the reliability of our results differed significantly from MZ probands from con- sorium pedigrees of nonwin siblings (P<.05 for all comparisons). Measures indicating relatively extreme homo- sexuality, such as age of first homosexuality, were positively associated with sexual orientation for men, and the self-designation of lesion/homosexual as opposed to bisexual. None of these variables was strongly associated with controversial issues of concern (P>.25). Rather, the study of homosexuality is not expected to have an indicator of genetic loading per se. However, if these results are the consequence of model redundancy, diminishing the statistical power of relevant analyses.

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**Other Similarities Between MZ Twins**

Another approach to the problem of the pathways from genotype to phenotype concerns the similarity of MZ twins for characteristics related to sexual orientation. If differences from concordant pairs tend to be similar for other important variables, such as degree of CGN, then it is more likely that these differences, by chance, are due to the environment shared by twins. Covariates from concordant pairs may reflect a greater variance in the environment, but if the concordance from discordant pairs is not significantly different from that in concordant pairs, then the adolescent Kinsey score, and age of first homosexuality is a candidate for a heritability bias or a heritability bias of the type that has been obtained in the present study by this method. The estimated bias of the bias that we have obtained is that the bias is not appreciable. To test this hypothesis, the bias of the bias that we have obtained is that the bias has no implications. To take into account the extent to which overrepresentation of this phenomenon to be the result of the test we have undertaken, the bias of the bias that we have obtained is that the bias is not appreciable. To test this hypothesis, the bias of the bias that we have obtained is that the bias is not appreciable.

**COMMENT**

Ascertainment Bias

The primary threat to the validity of the central finding, that genetic factors play a role in the origin of female sexual orientation, is ascertainment bias. Because probands were not obtained through systematic sampling, and particularly given the evidently low probability of ascertainment, it is not clear that patterns of volunteering yielded misleading results. However, all kinds of as- certainment bias would be difficult to eliminate. For example, our heritability analyses examined the effects of concordant pairs who did not have gay relatives, and found that heritabilities remained significant when a wide range of criteria were used that made the known of bias. Moreover, concordant-dependent bias cannot lead to a false finding of nonzero heritability, although it does have the potential of leading to zeroheritability. Regarding the magnitude of concordance-dependent bias in the present study, it is noteworthy that the concordance rate for DZ twins (16%) was lower than for concordant nonwin siblings of homosexual probands by Bailey and Benishay (12%) and that it found for nonwin siblings in the present study (14%). It is less plausible that the latter rates were serious- ly biased. Bailey and Benishay recruited subjects who were initially blind to the study’s focus on familiarity. Twin probands in the present study were aware of its focus on twins and, hence, might be expected to consider their co- twins’ sexual orientation when answering our questions. It is highly likely that they would weigh their other siblings’ orientations. Despite these differences, all three rates were similar, suggesting that at least for DZ twins, concordance-dependent bias was not large.

Serious errors could have resulted if concordant-dependent bias differed among the three groups. For instance, if DZ twins are less susceptible than MZ twins to concordance dependent bias, this suggests that our results could be due to ascertainment bias rather than to con- ciliation. However, the most likely explanation is that ascertainment bias was probably under-estimated, diminishing the statistical power of relevant analyses.

Arch Gen Psychiatry-Vol 50, Mar 1993

Sexual Orientation in Women—Bailey & Eti

Arch Gen Psychiatry—Vol 50, Mar 1993
Equivalence-Weights Assumption

The validity of our method to study genetic variation depends on one key assumption: Because the method uses regression coefficients to estimate genetic effects, one must be assured that the trait-relevant environment is equally similar for MZ and DZ twins and adoptive siblings. Although this assumption is not testable in the context of twin research, available research supports its validity, at least for traits studied so far.3,22 For instance, although some MZ twins are treated quite similarly by their parents in predictable ways (eg, being dressed alike), these MZ twins are no more similar in intelligence and personality than those treated dissimilarly by their parents. Twins whose zygosity is masked by their parents are as phenotypically similar as twins whose zygosity is correctly assessed. Although the equivalence-assumption has generally been supported, further genetic studies of sexual orientation should examine the assumption directly.

Implications for the Causes of Sexual Orientation

Heredity remained significant and appreciable (>25%) for all sets of assumptions examined, although the assumptions explored herein do not exhaust the realm of possibilities. The findings indicate that at least a portion of the variance of sexual orientation is due to genetic influences in our sample of twins. The findings provide some support for the hypothesis that genes play a role in sexual orientation, though the extent of the role is not well understood. The findings also suggest that environmental factors may play a role in the development of sexual orientation, and that the interaction between genetic and environmental factors is important in the expression of sexual orientation.

References


