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Biological Foundations of Sexual Orientation

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This chapter explores possible causes of sexual orientation. As does any psychological or behavioral trait, sexual orientation has two broad types of causes, proximate and ultimate (Mayr, 1958, 1988). Proximate causes include immediate neurophysiological factors and developmental phenomena, such as early hormone signaling, both of which are influenced by the interaction of genotype with environment. Ultimate causes are evolutionary causes and address the issue of why natural selection favored a particular phenotype or set of phenotypes over the range of alternatives that existed ancestrally.

In recent decades there has been a profusion of research into both proximate and ultimate causes underlying variation in sexual orientation (e.g., Blanchard & Bogaert, 1996; Bailey, Dunne, & Martin, 2000; Vasey & Vanderlaan, 2010). The latter line of inquiry is built upon evidence suggesting that there are genes predisposing individuals to homosexuality, and it seeks to explain how such genes might be maintained despite fitness costs associated with homosexuality in terms of reproductive success. Multiple hypotheses have been proposed, with modest supporting evidence. Research into proximate causation has identified neuroanatomical differences between gay and heterosexual individuals, effects of prenatal hormonal signaling on sexual orientation, and associations between the number of older brothers men have and their sexual orientation. Our goal is to illuminate both proximate factors influencing the spectrum of sexual orientations and ultimate causes maintaining this variation during the evolutionary history of our species.

HOW PREVALENT IS HOMOSEXUALITY?

Sexual orientation, according to LeVay and Baldwin (2009, p. 453), "is the dimension of personality that describes the balance of our sexual attraction to the two sexes." This definition focuses on a psychological construct, attraction to males and females, as opposed to describing sexual behavior or identity, which are correlated with, but not identical to, attraction. Because attraction captures the essence of orientation (i.e., having a particular direction), and is perhaps less likely than behavior or identity to be influenced by cultural and societal norms, most researchers studying the biology of sexual orientation examine sexual attraction.

Historically, the most common method of assessing sexual orientation has been the Kinsey Scale, which ranges from zero (exclusively heterosexual) to six (exclusively homosexual) and can be used to measure four dimensions: attraction, fantasy, behavior, and self-identification (Kinsey, Pomeroy, & Martin, 1948). Studies vary in their statistical treatment of this scale, though a common practice is to create three discrete categories, classifying individuals scoring 0 or 1 as heterosexual, those scoring 2 to 4 as bisexual, and those scoring 5 or 6 as homosexual (Rieger, Chivers, & Bailey, 2005).

Sexual attraction and fantasy are thought to be the most temporally stable of the four dimensions recognized by Kinsey et al. (1948), with self-identification and behavior more susceptible to change throughout the course of life (Klein, Sepekoff, & Wolf, 1985). Because of this, operationalizing sexual orientation as attraction tends to result in more conservative prevalence rates of homosexuality. This method of assessment also shows a sex difference concerning frequency distributions: In females the distribution of sexual attractions appears unimodal and continuous, with the majority of women scoring near the exclusively heterosexual end of the scale and decreasing frequencies as we move toward the exclusively homosexual end (Bailey, Dunne, & Martin, 2000). The

distribution of orientation in males, by contrast, appears bimodal, with the majority scoring near the exclusively heterosexual end and another, smaller mode near the exclusively homosexual end, with few in between (Bailey et al., 2000).

Initial research on genital arousal found that men who reported bisexual attraction tended to exhibit greater arousal to one sex, usually men, rather than similar arousal to both sexes (Rieger et al., 2005). However, more recent research (Rosenthal, Sylva, Safron, & Bailey, 2011) has found that men who report both bisexual attraction and past sexual behavior with men and women tend to exhibit similar genital arousal to both male and female sexual stimuli. One explanation is that these men's attraction to both sexes incited them to seek mating opportunities with both men and women. Another, not mutually exclusive, explanation is that their histories of homosexual and heterosexual behavior heightened their attraction and arousal to both sexes. Further research is needed to resolve this (see Janssen, McBride, Yarber, Hill, & Butler, 2008, for further discussion). Other research has shown that women are generally more aroused by images of sexual activity than are men, whose arousal seems more contingent on the sex of the erotic stimulus (Chivers, Seto, & Blanchard, 2007). Lesbians exhibit significantly more genital arousal to sexual stimuli of their preferred sex than do heterosexual women (Chivers, Rieger, Latty, & Bailey, 2004). In terms of the magnitude of the contrast between arousal to preferred versus nonpreferred sex, lesbians are intermediate between men and heterosexual women (Chivers et al., 2004; Rieger et al., 2005).

PROXIMATE CAUSATION

Homosexual attraction seems to exist at similarly low frequencies across human societies (e.g., Dawood, Bailey, & Martin, 2009; Sandfort, 1998, but see Laumann, Gagnon, Michael, & Michaels, 1994). Chandra, Mosher, and Copen (2011) and Gates (Chapter 6, this volume) provide the most recent estimates for the United States. Although variability in frequency estimates may partly be attributed to differences in questions asked, estimates rarely exceed 10% (Diamond, 1993). This cross-cultural consistency suggests that same-sex attraction may not be chiefly the product of learning or socialization (Haider-Markel & Joslyn, 2008). Rather, cross-cultural similarities suggest more intrinsic causes, an idea that has in recent decades directed biological research concerning the causes of sexual orientation. This research has focused on four interrelated areas of study: behavior genetics, prenatal sex hormone exposure, neuroanatomy, and, in males, fraternal birth order. Each of these will be discussed in turn.

Behavior Genetics

Some of the most convincing initial studies of the biological basis of sexual orientation were the product of the emerging field of behavior genetics (Kallmann, 1952). This line of research focusing on homosexuality continued in ensuing decades (e.g., Heston & Shields, 1968; Rainer, Mesnikoff, Kolb, & Carr, 1960), with comparable findings from study to study. For instance, in a review paper, Pillard et al. (1981) found that both lesbians and gay men were more likely than heterosexual men and women to have gay siblings, with monozygotic twins yielding the highest concordance rates in orientation, as would be expected assuming a genetic predisposition to the trait. Shortly thereafter, Pillard et al. (1982), studying a sample of 50 heterosexual and 50 homosexual men, found that roughly 25% of the gay men's brothers were also reported to be gay. Pillard and Weinrich (1986) found gay men reported having roughly four times as many gay brothers as heterosexual men did, suggesting a familial aggregation of genes underlying the trait's variation in men.

Bailey and Benishay (1993) found lesbians had a higher proportion of lesbian sisters and (though nonsignificantly) a higher proportion of gay brothers than heterosexual women. These data suggest that male and female homosexuality may be cofamilial to some degree, a conclusion also suggested by Bailey and Bell (1993). The question of whether this is true to the same degree for males was pursued several years later, with the finding of Bailey et al. (1999) that between 7% and 10% of brothers and 3% and 4% of sisters of gay men were gay themselves. Both of these ranges are higher than expected, suggesting a role for familially aggregated genes. On the other hand, Bailey et al. (1995) found a negative result when exploring whether young men are more likely to be gay if their fathers are: Fewer than 10% of the sons were gay.

The above studies reporting cofamiliality of homosexual orientation suggest a genetic component, but twin studies provide stronger evidence of heritability. For instance, Kendler et al. (2000)

found that monozygotic twins of both sexes were concordant for homosexuality (32%) more often than were dizygotic (13%) or nontwin siblings. In the largest twin study conducted to date, Bailey et al. (2000) used a carefully ascertained twin sample from the Australian Twin Registry to establish heritability estimates for sexual orientation in men and women. This study reported 20% of male MZ twins concordant versus 0% of DZ twins, and 24% of female MZ twins versus 10.5% of DZ twins. In a recent large twin study, Langstrom, Rahman, Carlstrom, and Lichtenstein (2010) estimated a heritability of 0.34 to 0.39 for men and 0.18 to 0.19 for women. In general, although figures may differ slightly from study to study, the trend is clear: as the genetic relatedness of siblings increases, so does their likelihood of concordance for orientation.

Hamer and his colleagues (1993) proposed the first candidate gene for male homosexuality. Hamer's research team found an increased prevalence of homosexuality among male kin on the maternal side, suggesting that male homosexuality may be a sex-linked trait. This led Hamer and his colleagues to examine the X-chromosome and to find that gay brothers share markers at the Xq28 locus much more frequently than would be expected by chance (Hamer et al., 1993). Although Hamer's research team was able to replicate its initial result (Hu et al., 1995), other attempts at replication (Rice, Anderson, Risch, & Ebers, 1999; Sanders et al., 1998) have been unsuccessful. Although Sanders et al. (1998) reported inconclusive evidence of linkage to Xq28, a notable negative finding was that of Rice et al. (1999), who examined four markers on a 12.5-centimorgan region of Xq28 (DXS1113, BGN, Factor 8, and DXS1108) in search of further evidence that male homosexuality is sex-linked. To this end, the researchers used a sample of 52 pairs of siblings, with both members of each pair self-identifying as gay. Because DNA samples from these siblings' mothers were not easily obtainable, the markers genotyped for the siblings were compared with controls from the population. Results indicated that none of the markers in question was shared more often than would be expected from population base rates. The reasons for the discrepancy between this study and the previous studies from Hamer's laboratory are unclear. More recently, Mustanski et al. (2005) also failed to replicate the positive Xq28 finding but reported linkage findings for 7q36, 8p12, and 10q26. However, this study has not been replicated. The first two of these genes have approximately the same maximum likelihood estimation score for maternal and paternal contributions, possible evidence against male homosexuality as a sex-linked trait. Candidate genes continue to be suggested, and the issue is far from resolved.

In addition to the linkage studies described above, two association studies of male sexual orientation have been conducted to date. Unlike linkage studies, which can search the entire genome and examine genetic markers rather than genes, association studies explore the relation between genetic variation at a particular candidate locus and phenotypic variation. Macke et al. (1993) found no significant differences between gay and heterosexual men in the distributions of variants of the androgen receptor gene. Dupree et al. (2004) found no associations between variation in the gene encoding the aromatase enzyme, or differences in its expression, and sexual orientation in men. However, although aromatase is instrumental in masculinizing the brains of some mammals, including laboratory rodents, this may not be the case in humans (Zuloaga, Puts, Jordan, & Breedlove, 2008).

As is evident, behavior genetics has made substantial contributions to the literature on sexual orientation during the past three decades. Most impressive is the repeatedly observed trend of increasing likelihood of concordance for both male and female homosexuality with increasing genetic relatedness between siblings. However, the search for "gay gene(s)" to date has been chiefly an unsuccessful endeavor, lacking replicable results. Future studies are needed to illuminate the genetics of sexual orientation.

Sex Hormones

Like research into the behavior genetics of sexual orientation, studies examining associations between sexual orientation and sex hormone exposure have helped to shed light on its biological components. Early research suggesting links between adult sexual orientation and both prenatal sex hormone signaling (e.g., Ward, 1972; Ellis et al., 1988; Bailey & Pillard, 1991) and gender-related behavior during childhood (Green, 1985) spawned research into possible associations among all three phenomena. Because gender atypicality during childhood may be associated with adult homosexuality, if prenatal hormone exposure affects childhood gender atypicality, this might suggest a link between prenatal sex hormones and adult homosexuality.

Childhood gender nonconformity (CGN) is among the best predictors of adult homosexuality for men, both in retrospective (e.g., Whitam, 1977) and in prospective (e.g., Money & Russo, 1979) studies. For example, Money and Russo (1979) followed 11 gender nonconforming boys in a longitudinal study and obtained much the same findings as had been previously found (e.g., Whitam, 1977). The boys were selected on the basis of (1) "exceptional interest in dressing in girls' clothing," (2) "avoiding play activities typical of boys and preferring those of girls," (3) "walking and talking more like girls than boys," and (4) "stating overtly the wish to be a girl." The boys were prepubertal at the commencement of the study and none exhibited homosexual behavior. In early adulthood all of the boys were found to be gay. Zuger (1984) examined 55 boys with "early effeminate behavior." On follow-up, 64% of the original participants were nonheterosexual, 6% were heterosexual, and in 18% there was either insufficient information from follow-up meetings or too short a follow-up period to warrant categorization of sexual orientation. [See Bailey & Zucker (1995) for a meta-analysis of studies on this topic.]

Further support for the association between CGN and adult homosexuality comes from a study of 44 gender-nonconforming boys and 34 gender-conforming boys (Green, 1985). The boys were matched on "age, gender, and sibling sequence" and the parents on "race, religion, educational level, and marital status." Of the 44 gender-nonconforming boys, 30 were gay or bisexual when scored on the fantasy dimension, and of these, 24 were gay or bisexual in terms of their sexual behavior. Of the boys in the gender-conforming group, all were heterosexual by both measures. More recent research (Lippa, 2008) has found similar results in an ethnically diverse sample of nearly 1000 men from the United States.

Other research has taken a novel route in pursuit of a better understanding of this issue. Rather than relying on self-reports of gender-nonconforming behavior or retrospective accounts of CGN, Rieger et al. (2008) utilized observation of home videos. Gay male, lesbian, and heterosexual adults were shown video footage of both children who grew up to be lesbian or gay or heterosexual. Children who grew up to be lesbian or gay were perceived to be significantly more gender-nonconforming than were other children, and these perceptions accorded with self-reports of the adults from the videos. Finally, the association between CGN and adult homosexuality has also been observed across cultures. Whitam and Mathy (1991) found results similar to those reported above in Brazil, Peru, the Philippines, and the United States for females.

Results of these studies suggest that CGN and adult homosexuality may be correlated, at least in males. What might be responsible for the association? One answer may involve organizational effects of prenatal or early postnatal exposure to sex hormones on brain regions involved in sexual orientation and other sexually differentiated psychological traits. Research into this possibility employs both "natural experiments" and biomarkers in an effort to establish connections between early sex hormone exposure and sex-atypical behavior and psychology.

Natural experiments. Some males with sex-typical prenatal androgen exposure have undergone gender reassignment shortly after birth due to damage to the penis that required its removal, or to resolve abnormal differentiation of the genitals, as in a condition called cloacal exstrophy. Such males raised as females frequently report sexual attraction to females as adults, with one sample of 35 males all showing adult attraction to females (Mustanski, Chivers, & Bailey, 2002; Reiner & Gearhart, 2004). This suggests that prenatal developmental events, including those dependent on sex hormones or early developmental issues, may have effects on sexual orientation that persist despite discordance with the assigned gender role.

Another condition, congenital adrenal hyperplasia (CAH), is characterized by excess prenatal androgen exposure. Compared to unaffected female controls, females with CAH tend to perform at more male-typical levels on sexually differentiated spatial cognitive tasks (Puts, McDaniel, Jordan, & Breedlove, 2008) and tend to show more male-typical childhood play patterns and adult vocational interests (Berenbaum, 1999; Hines, Brook, & Conway, 2004). CAH women are also more likely than non-CAH women to be lesbian or bisexual (Ehrhardt, Evers, & Money, 1968; Hines et al., 2004; Zucker et al., 1996). For example, Hines et al. (2004) found a statistically significant difference in sexual orientation between CAH and non-CAH women, with 31% of CAH women indicating their sexual behavior during the year preceding the study to be with women or with both men and women.

By contrast, all of the non-CAH women reported their sexual behavior to have been exclusively or mainly with men. Thus, these findings suggest that increased prenatal exposure to androgens masculinizes both gendered behavior and sexual orientation among girls and women; no such effects have been observed among boys or men.

In addition, 46 *XY* (i.e., chromosomally male) individuals with complete androgen insensitivity syndrome (CAIS) are similar to unaffected female controls in their sexual orientation (Hines, Ahmed, & Hughes, 2003; Money, Schwartz, & Lewis, 1984; Wisniewski et al., 2000). This is remarkable because individuals with CAIS develop testes that remain undescended, and produce normal-to-high male levels of testosterone (Imperato-McGinley et al., 1982). Individuals with CAIS are nonetheless phenotypically female because they lack functional androgen receptors and therefore do not undergo the virilization experienced by non-CAIS individuals (Imperato-McGinley et al., 1982). Their female-typical attraction to men is consistent with the hypothesis that androgen signaling is critical in developing sexual attraction to women. However, this evidence may be confounded by other developmental factors, especially socialization effects. For example, sexual orientation in individuals with CAIS is consistent with gender of rearing. Thus, the rearing environment, rather than the absence of androgen-signaling in the brain, may account for sexual orientation in CAIS women. Such women are socialized as girls and behave in ways culturally appropriate for individuals with a female phenotype. The male-typical gender role behavior of girls with CAH may elicit psychosocial experiences that influence the development of their sexual orientation (but see Pasterski et al., 2005).

Biomarkers. Other research has focused on anatomical differences between males and females that are thought to result from differential exposure to sex hormones during early development. Martin and Nguyen (2004) found that arm, hand, and leg bones that become dimorphic prior to puberty differ not only between males and females but also between androphilic individuals (i.e., heterosexual women and gay men) and gynephilic individuals (i.e., heterosexual men and lesbians). The researchers interpreted this result as reflecting less than typical prepubertal androgen exposure in androphilic men and higher than normal prepubertal androgen exposure in gynephilic women.

Sex hormone exposure may influence not only the development of homosexuality, but also variation in sexual orientation among gays and lesbians. For example, an association has been found between "butch" (masculine-acting) lesbianism and (1) a higher (more male-typical) waist-to-hip ratio (Singh, Vidaurri, Zambarano, & Dabbs, 1999) and (2) increased levels of baseline testosterone within lesbian couples, but not among lesbians generally (Pearcey, Docherty, & Dabbs, 1996).

One of the most heavily researched lines of inquiry into the role of sex hormones on sexual orientation is the association between sexual orientation and the ratio of the second to fourth finger lengths (2D:4D). Because variation in 2D:4D probably results from differences in prenatal sex hormone signaling (Breedlove, 2010; Manning, Scutt, Wilson, & Lewis-Jones, 1998), 2D:4D is frequently used as a proxy for prenatal sex hormone exposure. There has been a recent increase in such research, largely because it is relatively uncomplicated to conduct and is linked in no obvious way to socialization or enculturation, thus decreasing the likelihood that these processes will confound any observed effects. However, the degree to which 2D:4D can elucidate the ontogeny of sexual orientation is unclear. For example, Robinson and Manning (2000) provided evidence that 2D:4D is lower in gay males than it is in heterosexual males, an unexpected pattern given the well-established finding that heterosexual males have lower 2D:4D than heterosexual females (Grimbos, Dawood, Burriss, Zucker, & Puts, 2010; Manning et al., 1998). Manning et al. (2007), however, found *higher* 2D:4D ratios among gay men, whereas Voracek et al. (2005) found *no* difference between gay and heterosexual men.

Among women, lesbians (e.g., Hall & Love, 2003), and specifically "butch" lesbians (Brown, Finn, Cooke, & Breedlove, 2002), have been found to possess a lower (more masculine) 2D:4D ratio than heterosexual women and than "femme" (feminine-acting) lesbians. Although Lippa (2003) found no 2D:4D differences between lesbians and heterosexual women in a large sample, the most recent systematic review of previous research on this topic (Grimbos et al., 2010) concluded that the preponderance of evidence suggests that there is a difference in 2D:4D between lesbians and heterosexual women but not between gay and heterosexual men. This meta-analysis utilized data from 21 studies covering the years 2000 to 2009, including

18 male and 16 female samples comprising 1618 heterosexual men, 1503 gay men, 1693 heterosexual women, and 1014 lesbians. Thus, findings on 2D:4D ratios overall suggest that early androgen signaling is associated with sexual orientation, at least in women.

The ratio of second to fourth finger length is not the only biomarker to display a sexual orientation difference. A meta-analysis (Lalumiere, Blanchard, & Zucker, 2000) found that gay men were 34%, and lesbians 91%, more likely than heterosexual men and women to be left handed or ambidextrous. Because handedness does not appear to be dependent upon socialization and is fixed from an early age, it is thought to be under the control of perinatal neurodevelopmental effects (Hepper, McCartney, & Shannon, 1998; Hepper, Shahidullah, & White, 1991). One hypothesis posits that differential exposure to testosterone prenatally shifts cerebral dominance to the right hemisphere, which could explain why heterosexual males and lesbians are more likely than heterosexual women to be non-right-handed. A related finding is that of more masculine otoacoustic emissions (sound waves emanating from the inner ear) among lesbians, explained by researchers as the product of increased exposure to androgens prenatally (McFadden & Pasanen, 1998, 1999).

Thus, multiple converging lines of evidence provide some support for the hypothesis that variation in prenatal androgen signaling (sensitivity to androgens and/or androgen production) accounts for some variation in sexual orientation among females. The causes of variation in sexual orientation among males are less clear, although evidence strongly suggests the importance of early, probably prenatal or early postnatal, developmental events.

Neurobiology

Sex steroids exert their influence by regulating gene expression in their target tissues (Nelson, 2005). For gene expression changes to influence sexual orientation, the target tissues would presumably be the nervous system, and such changes would affect neural development. In other words, we would expect the neuroanatomy and/or neurophysiology of males and females, as well as that of gay and heterosexual individuals, to differ. An obvious place to look for such differences is the brain.

LeVay (1991) investigated differences in sexual orientation in the interstitial nuclei (i.e., groups of neuronal cell bodies) of the anterior hypothalamus, as there were known human sex differences in the size of these structures, and this brain area relates to sexual behavior in laboratory animals. In a sample of cadavers from 19 gay men, 16 presumably heterosexual men, and six presumably heterosexual women, LeVay found the third nucleus (INAH3) to be roughly twice as large in heterosexual men as in gay men or heterosexual women. He was unable to procure a large enough sample to test for a similar difference in sexual orientation in women. It is possible that LeVay's results were confounded by the fact that all of the gay men, six of the 16 heterosexual men, and one of the six women in his sample had died of AIDS. However, LeVay found that the six heterosexual men who had died of AIDS had an INAH3 that did not differ in size from that of uninfected heterosexual men. This result has been replicated with moderate success, with Byne and colleagues (2001) also reporting a nonsignificant trend toward a smaller INAH3 in gay than in heterosexual men. That said, the neuronal number was about the same in INAH3 between the two groups and AIDS was shown to influence the size of this structure.

Other research on neuroanatomical differences between men and women of different sexual orientations has focused on the hypothalamus. Swaab and Hofman (1990) demonstrated that the suprachiasmatic nucleus (SCN) was 1.7 times as large and contained 2.1 times as many cells in a sample of gay men as in a sample of randomly chosen men. Allen and Gorski (1992) found the anterior commissure to be 34% larger in gay than in heterosexual men.

Although this research suggests differences in sexual orientation in the structure of the hypothalamus, it is impossible to ascertain from these data whether hypothalamic structure influences sexual orientation, sexual behavior influences hypothalamic structure, or whether the two are linked because of a third variable. Even if the first of these possibilities is correct, the overlap between the gay and heterosexual men in the anatomy of these structures suggests that male sexual orientation may not vary as a result of any single neuroanatomical difference.

Research using positron emission tomography (PET) scans indicates that certain aspects of brain functioning differ between gay and heterosexual

individuals. For instance, the hypothalamus was activated in gay, but not heterosexual, men after inhalation of putative male pheromones (Savic, Berglund, & Lindstrom, 2005). This trend of sex-atypicality in brain activation after inhalation of pheromones has been shown in lesbians as well (Berglund, Lindstrom, & Savic, 2006). Furthermore, there is evidence that gay men (Hu et al., 2008; Safron et al., 2007) exhibit different brain activation from heterosexual men when exposed to visual sexual stimuli.

Safron et al. (2007) showed gay and heterosexual men male–male and female–female sexual stimuli, as well as images of sexually neutral stimuli. Participants viewed these images while undergoing functional magnetic resonance imaging (fMRI). When viewing sexual images of their preferred sex, men demonstrated increased activity in several brain regions. Hu et al. (2008) obtained similar results, but also showed a difference between the brain regions activated in gay and heterosexual men upon exposure to stimuli of their preferred sex. Of course, the role of past experiences cannot be ruled out as influencing neuroanatomy to the extent that brain regions in gay and heterosexual individuals differ with respect to activation during sexual arousal. Similar research has yet to be done with women.

Other research suggests that, like men, lesbians possess less gray matter (parts of the central nervous system composed largely of neuronal cell bodies) in areas of the perirhinal cortex than do heterosexual women (Ponseti et al., 2007). This finding is important because the perirhinal cortex is located near brain regions (entorhinal cortex, hippocampus, parahippocampal gyrus, and amygdala) involved in olfactory and spatial processing, which have been shown to exhibit differences in sexual orientation such as slower spatial learning and reduced mental rotation ability in gay than in heterosexual men (Rahman & Koerting, 2008; Rahman & Wilson, 2003). Yet other research has shown that the cerebrum of heterosexual men and lesbians (i.e., gynephiles) is asymmetrical in a rightward direction, whereas the cerebrum of gay men and heterosexual women (i.e., androphiles) is not asymmetrical, and that both gay men and lesbians show different amygdala connections than do heterosexual men and women (Savic & Lindstrom, 2008). Of course, it is unclear whether these neuroanatomical phenomena cause variation in sexual orientation, whether some aspect of sexual behavior causes these neuroanatomical differences, or whether these differences are not causally related to sexual orientation at all.

Research on the topic of neuroanatomical differences between lesbian or gay and heterosexual individuals has thus yielded repeated demonstrations of brain differences between the two groups. The differences in brain structure reported have generally indicated that gay men resemble heterosexual women and lesbians resemble heterosexual men.

Fraternal Birth Order

The last of the major lines of research on biological components of sexual orientation concerns a phenomenon that may at first glance seem to have little connection to sexual orientation: birth order. Specifically, a repeated finding has been that the number of a man's (but not a woman's) older brothers increases his likelihood of being gay, each older brother increasing the odds by approximately 33% above the base rate of 2–3% (Blanchard & Bogaert, 1996). This is called the fraternal birth order effect. With a host of studies since the mid-1990s replicating this finding (reviewed in Blanchard, 2008; Bogaert & Skorska, 2011), the fraternal birth order effect is one of the most well-established proximate correlates of sexual orientation.

What is it about the number of older brothers that relates to a man's chances of being gay? One hypothesis is socialization—for instance, that being reared in a home with older brothers in some way "demasculinizes" a boy. This appears not to be the case, as only the number of biological brothers from the same mother predicts a man's likelihood of homosexuality, regardless of the duration of rearing together, or even whether the brothers were reared together at all (Bogaert, 2006). Moreover, no other category of sibling, including older stepbrothers and half-brothers through the father, has an influence or correlation (Bogaert, 2006), nor does spacing of siblings (Blanchard & Bogaert, 1997) or parental age (Blanchard & Sheridan, 1992). Gay men with older brothers have also been shown to have lower birth weights than have heterosexual men with older brothers (Blanchard & Ellis, 2001), and since birth weight is contingent on gestational events, this suggests that whatever phenomenon is responsible for the trend exerts its influence early, during gestation.

Blanchard and Klassen (1997) proposed the maternal immune hypothesis to explain the fraternal birth order effect. According to the hypothesis, when a mother gives birth to a son, maternal and fetal blood mix, and the mother's immune system is exposed to Y-linked (male-specific) antigens. The mother produces antibodies to these male-specific antigens, which can cross the placental barrier in later pregnancies. These antibodies then in some as yet unknown way affect the neural development of every subsequent male fetus (see also Puts, Jordan, & Breedlove, 2006). Because the production of antimale antibodies is bolstered by each subsequent delivery of a son, the mother's immune system can "remember" the number of sons she has previously delivered, increasing the likelihood of later homosexuality by about one-third of the population base rate with each successive son. This theory is admittedly speculative at this point, though it is the only widely accepted explanation of the fraternal birth order effect (Bogaert & Skorska, 2011).

Two recent estimates of the percentage of male homosexuality attributable to the fraternal birth order effect are 15.1% (Cantor, Blanchard, Paterson, & Bogaert, 2002) and 28.6% (Blanchard & Bogaert, 2004). Thus, even among proponents of this theory, most male homosexuality (and all of female homosexuality) is not explained by this phenomenon. Nonetheless, the fraternal birth order effect remains the best-supported of all proximate explanations for the etiology of homosexuality.

ULTIMATE CAUSATION

The discussion thus far has focused on causal agents at the proximate level, including evidence of genes underlying variation in sexual orientation. The prospect of "gay genes" is intriguing from the perspective of evolutionary biology, as lesbians and gay men tend to produce fewer offspring than do heterosexual men and women (Bell & Weinberg, 1978). Even allowing for cultural stigma concerning homosexuality or social pressures to marry and procreate, it is doubtful that lesbians and gay men in any time or place would have equaled the reproductive output of their heterosexual counterparts. Hence the evolutionary conundrum: If there are genes that predispose their bearers to developing a homosexual orientation, and if these genes tend to restrain reproduction, why has natural selection not eliminated them? Several theories have suggested an answer.

Kin Selection

Perhaps the best known of these theories involves kin selection (Hamilton, 1964a, 1964b). E. O. Wilson put the idea this way:

> The homosexual members of primitive societies may have functioned as helpers, either while hunting in company with other men or in more domestic occupations at the dwelling sites. Freed from the special obligations of parental duties, they could have operated with special efficiency in assisting close relatives. Genes favoring homosexuality could then be sustained at a high equilibrium level by kin selection alone. (Wilson, 1975, p. 555)

The assumption is that the "gay genes" reside not only in the lesbians and gay men themselves, but in their close genetic relatives. However, only in certain combinations and/or under particular environmental conditions do these genes increase the probability that an individual will be lesbian or gay, which is why the kin do not possess this trait and the lesbian or gay individuals do. When the kin reproduce (with greater success, aided by their altruistic gay relatives), they replicate copies of the gay genes and thus perpetuate the trait despite its detrimental effect on individual reproductive success. In this way, according to the theory, a lesbian's or gay man's individual reproductive fitness may be decreased, but the reproductive fitness of the gay genes is not.

Research has provided mixed evidence to support this hypothesis. For example, Bobrow and Bailey (2001) tested the theory in an American sample and found no evidence in support of it. They gave gay and heterosexual men questionnaires concerning sentiments and behavior toward kin and found no evidence that gay men behaved more altruistically toward kin than did heterosexual males. In fact, gay men reported giving *less* money than did heterosexual men to oldest and youngest siblings. Similar findings were obtained by Rahman and Hull (2005) in a British sample. These results contradict the central prediction of the kin selection theory. Of course, the United States and Britain are in important respects not representative of the environment in which humans spent the majority of their evolutionary history. Western lesbians and gay men may be more (1) geographically separated and (2) emotionally estranged from kin than

are non-Western lesbians and gay men (Bobrow & Bailey, 2001), weakening any tendency they may have to behave more altruistically toward relatives. Because of this, supporting evidence for the kin selection theory, if such evidence exists, may be difficult to find in such a sample.

In light of this, Vasey et al. (2007) conducted a study similar to that of Bobrow and Bailey (2001) in which the researchers examined a culturally recognized category of gender-variant male, the *fa'afafine* of Independent Samoa, who live in conditions that may, in some respects, be more similar to those of our evolutionary past. The researchers found no difference between gynephilic and androphilic males (i.e., heterosexual men and *fa'afafine*) with respect to "overall generosity or financial resources given to kin." However, androphilic males indicated greater levels of "avuncular tendencies" than did gynephilic males. These results prompted Vasey and his colleagues to stress the importance of studying evolutionary predictions in social environments thought to be more similar to those in which our species spent the majority of its evolutionary history. In Independent Samoa, for instance, members of extended families, *aiga*, tend to be geographically clustered near each other, facilitating frequent contact. Furthermore, because the *fa'afafine* have a recognized and unstigmatized place in Samoan culture, they suffer no noticeable estrangement from kin. In Samoa, the researchers note, male androphiles without children of their own have more time and resources to invest in nieces and nephews. To demonstrate that the avuncular tendencies of *fa'afafine* differ from those of heterosexual males, it is necessary to compare childless heterosexual men with childless *fa'afafine*. Vasey and Vanderlaan (2010) found that *fa'afafine* indeed display more altruistic behavior toward nieces and nephews than do childless heterosexual males. Moreover, heterosexual males with and without children did not differ in the extent of their avuncular tendencies, nor was there a negative relationship for heterosexual males between number of children sired and avuncular tendencies. These findings are consistent with the hypothesis that male homosexuality is an adaptation for kin-directed altruism, but they are of course limited to a single cultural group.

However, the kin selection hypothesis for homosexuality may be undermined by the apparent inefficiency of homosexuality for this function. Given androphilic males' investment in pursuing and maintaining homosexual relationships, a lack of sexual motivation, rather than homosexuality, would seem a more efficient means of increasing investment in kin. Moreover, because individuals are twice as genetically related to their own offspring as they are to nieces and nephews, they would have to be exceptionally altruistic for the benefits of investing in nieces and nephews to offset the costs of forgoing reproduction. Finally, perhaps some trait other than homosexuality, for example, traditionally sex-typed "feminine" characteristics such as caring or empathy, causes *fa'afafine* to exhibit more altruism toward kin. Overall, the findings provide limited support for the kin selection hypothesis.

Pleiotropy

Genes may have different effects in different bodies, a phenomenon known as pleiotropy. A gene or collection of genes might propel one individual toward same-sex attraction, whereas the same gene or combination of genes might have a different effect in another individual. If there really are "gay genes," then the effects of such genes in heterosexual individuals may increase reproductive success, offsetting the costs to reproductive fitness incurred when the genes are in gay individuals.

Miller (2000) proposed that women prefer in men typically feminine attributes such as kindness and empathy, which may make men better fathers. According to Miller, men with an intermediate level of behavioral femininity would be desirable as long-term mates, gaining a reproductive advantage over more masculine or more feminine men. Consequently, selection would favor both alleles contributing to behavioral masculinity and alleles contributing to behavioral femininity. The most reproductively successful males might have an intermediate number of each. Due to recombination during sexual reproduction, some males would inherit more alleles contributing to behavioral masculinity, and some would inherit more alleles contributing to behavioral femininity, than is advantageous under natural selection. A small minority of males would inherit an extreme number of alleles contributing to behavioral femininity and would develop a homosexual attraction. Miller points to the correlation between psychological gender-atypicality and sexual orientation (Bailey, Nothnagel, & Wolfe, 1995; Bailey & Zucker, 1995; Green, 1985) in support of this hypothesis. In addition, gay men may have, on average, more feminine

fathers than do heterosexual men (Bell, Weinberg, & Hammersmith, 1981).

An advantage of this hypothesis is that it can be applied to both sexes. Regarding lesbians, Miller argues that although men may prefer physically and psychologically feminine women, our female ancestors may also have benefited from some psychological masculinity. For example, psychological masculinity may have helped women procure food and depend less on male support. As with Miller's hypothesis regarding male homosexuality, this hypothesis relies on an association between sexual orientation and gender nonconformity. As noted above, girls with CAH tend to be gender nonconforming in some ways and have a higher-than-base rate chance of being lesbian (Hines et al., 2004). Although consistent with some evidence, this hypothesis has at present little evidence to support it.

Two studies indicate greater reproductive success among the maternal but not paternal kin of gay men compared to heterosexual men (Camperio-Ciani, Corna, & Capiluppi, 2004; Iemmola & Camperio Ciani, 2009), a finding consistent with evidence that a gene contributing to male homosexuality may reside on the X-chromosome. At least one study has found greater reproductive success among both patrilateral and matrilateral kin of gay men (King et al., 2005). Rahman et al. (2008) found increased fecundity among maternal aunts of gay men only among white participants, with nonwhite heterosexual individuals displaying increased fecundity among most other kin types. In sum, there is some modest evidence (see also Zietsch et al., 2008) that if genes predispose some individuals toward homosexuality, they compensate for the associated decrement in reproduction by increasing the reproductive success of heterosexual individuals in which the same genes reside.

CONCLUSIONS

This chapter has discussed leading avenues of study into biological aspects of sexual orientation at both the proximate and ultimate levels of explanation. At this point in time, relatively little can be stated conclusively. Nevertheless, it is reasonably well-established that (1) both male and female homosexuality are at least partially heritable traits that are (2) sometimes associated with childhood gender nonconformity and (3) are found at similar frequencies across many culturally divergent populations. Early developmental (e.g., prenatal) events may influence within-sex variation in sexual orientation. Some evidence suggests that early developmental processes influencing female sexual orientation could include androgen signaling. Men's sexual orientation has been found to be associated with fraternal birth order, which could reflect a maternal immune response to male-specific antigens. Less is known at the ultimate level, though it appears that a pleiotropic genetic model is currently the most promising explanatory hypothesis. However, most theories at either level need not be mutually exclusive. Furthermore, the etiology of homosexuality is often studied separately by social and biological scientists, rather than from an interdisciplinary perspective, which may provide additional insights into the proximate and ultimate causes of sexual orientation.

What forms will this research take in the future? Replication of previous results is clearly necessary, and considerable additional research is required to clarify determinants of sexual orientation at the proximate level. Much of the needed research may come from genomics, neuroscience, and related fields. Rigorous exploration of the fraternal birth order effect, and specifically testing of the maternal immune hypothesis, might elucidate the etiology of sexual orientation for some individuals. It may well be the case that convincing tests of ultimate-level explanations for variation in sexual orientation must await a clearer understanding of proximate causes.

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