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TARGET ARTICLE

Prenatal Influences on Human Sexual Orientation: Expectations versus Data

S. Marc Breedlove[1]

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Abstract In non-human vertebrate species, sexual differentiation of the brain is primarily driven by androgens such as testosterone organizing the brains of males in a masculine fashion early in life, while the lower levels of androgen in developing females organize their brains in a feminine fashion. These principles may be relevant to the development of sexual orientation in humans, because retrospective markers of prenatal androgen exposure, namely digit ratios and otoacoustic emissions, indicate that lesbians, on average, were exposed to greater prenatal androgen than were straight women. Thus, the even greater levels of prenatal androgen exposure experienced by fetal males may explain why the vast majority of them grow up to be attracted to women. However, the same markers indicate no significant differences between gay and straight men in terms of average prenatal androgen exposure, so the variance in orientation in men cannot be accounted for by variance in prenatal androgen exposure, but may be due to variance in *response* to prenatal androgens. These data contradict several popular notions about human sexual orientation. Sexual orientation in women is said to be fluid, sometimes implying that only social influences in adulthood are at work, yet the data indicate prenatal influences matter as well. Gay men are widely perceived as under-masculinized, yet the data indicate they are exposed to as much prenatal androgen as straight men. There is growing sentiment to reject "binary" conceptions of human sexual orientations, to emphasize instead a spectrum of orientations. Yet the data indicate that human sexual orientation is sufficiently polarized that groups of lesbians, on average, show evidence of greater prenatal androgen exposure than groups of straight women, while groups of gay men have, on average, a greater proportion of brothers among their older siblings than do straight men.

Keywords Sexual orientation · Testosterone · Androgens · Birth order · Digit ratios · Otoacoustic emissions

Introduction

Most of us have wondered about the extent to which our behavior is a function of socialization, culture, and the learning process while growing up, and the extent to which our behavior can be attributed to more basic processes, what might be regarded as "biological" influences. Often this is posed as the relative contributions of nature versus nurture, or genetic versus environmental influences. But even a superficial understanding of the nature-nurture "debate," or of environmental regulation of gene expression, reveals these distinctions to be very difficult to sort out when you consider the details. So instead of those amorphous, difficult-to-define distinctions, it may be more productive to weigh the relative contributions of a more precisely defined duality, namely prenatal versus postnatal influences. The one thing we can say with some confidence is that prenatal influences cannot be attributed to social interactions, as the fetus is insulated from awareness of the behavior of any individuals (other than the mother, and her avenues of *social* influence, her voice perhaps, are relatively limited). If events before birth influence the individual's later behavior, at least we can say they could not have been *initiated* by the individual learning about behavior from others. Of course, to the extent prenatal events alter the individual's future behavior, that altered behavior may affect the way other people respond to the individual. From thence we spiral down the rabbit hole of iterative rounds of environmental influences on gene expression, which affects later experiences, which influences future gene expression

✉ S. Marc Breedlove
breedsm@msu.edu

[1] Neuroscience Program and Departments of Psychology, Integrative Biology, Michigan State University, 293 Farm Lane, Giltner Hall Room 108, East Lansing, MI 48824-1110, USA

and so on, indefinitely. What can we say about the relatively simpler question of prenatal versus postnatal influences on human behavior, specifically on sexual orientation?

Weighing Social Influences versus Prenatal Influences

Having spent most of my adult life investigating sex differences in behavior in non-human animals, I have wondered whether the results of animal studies have *any* relevance to sex differences in human behavior. We know that some sex differences in human behavior wax and wane over history and clearly are modified by culture. Some sex differences in mathematical performance, for example, have been steadily decreasing just in my lifetime, so that now there are some societies where girls perform better than boys, on average, in tests of math ability (Guiso, Monte, Sapienza, & Zingales, 2008). Still, there are other sex differences in human behavior that persist, at least for now. So it is fair to ask whether they are caused by the same sorts of prenatal events that lead to sex differences in animal behavior, which are well understood.

For over 50 years now, a relatively simple and powerful explanation of how sex differences in behavior arise in mammals—that sex differences in the brain are created through the same prenatal events that bring about sex differences in the body—has dominated the literature. Just as androgenic hormones like testosterone work early in life to form a male phenotype of the body, so too, do those hormones masculinize the developing brain to masculinize behavior in animals. And just as the relative absence of androgens early in life causes the body to develop a feminine phenotype, so too will the absence of early androgens result in the development of a feminine nervous system. From this perspective, the brain is just one more part of the body poised to detect a single, unifying signal: if androgens are high during a sensitive period, various cells and tissues distributed throughout the body should form a male phenotype, while if androgens are low they should form a female phenotype. There is a pleasing simplicity to the idea that a solitary signal, androgen, coordinates the feminine or masculine development of every part of the body, so that individuals that are going to reproduce as females have both the genitalia and behaviors to be successful in that role, and so do those that are going to reproduce as males.

That relatively simple but powerful *organizational hypothesis* (Phoenix, Goy, Gerall, & Young, 1959) has been applied to hundreds of published studies of animals and can account for the vast majority of sex differences not only in behavior, but in brain structure as well, at least in animals (Morris, Jordan, & Breedlove, 2004). Prenatal testosterone was even shown to masculinize the behavior of female monkeys (Eaton, Goy, & Phoenix, 1973), but interpretation of those studies was complicated by concerns about the extent to which the genitalia were also masculinized and so might have affected the social reaction of other monkeys (Goy & Phoenix, 1972). Thus, for me, the question remained whether the organizational hypothesis also holds true for the human brain and for sex differences in human behavior. Clearly there are influences other than prenatal androgens on human brain sexual differentiation—even recent history makes that obvious. The big question is whether there is *any* residual influence of prenatal gonadal steroids on human behavior at all.

To make this personal, while in graduate school and as a young professor, I happily studied the influence of early hormone exposure on the masculinization of the nervous system in non-human animals. There it was quite clear that I could make various parts the brain or spinal cord as masculine or feminine as I wanted simply by controlling how much testosterone the organism was exposed to. When the rat was exposed to androgen early in life, then the brain would be organized in a masculine fashion. If the individual was not exposed to testosterone early in life, then the brain would be organized in a feminine fashion. Eventually we found some brain regions that were sexually dimorphic not due to perinatal androgens, but were responding to androgens in adulthood (Cooke, Tabibnia, & Breedlove, 1999), but still hormones seemed to account entirely for the sex difference. Behavioral correlates of the sex differences in the structure of the brain were harder to demonstrate but, when found, were always consistent with brain changes (e.g., Cooke, Chowanadisai, & Breedlove, 2000; De Jonge et al., 1989; Gurney, 1982). Of course, as I published these studies and sought funds to pay for them, I always indicated that these processes might apply to human behavior. But in my private thoughts, I was very skeptical of the idea. Long after I was a Full Professor of Psychology, I had serious doubts about whether androgens working early in life have *any* influence whatsoever on the developing *human* brain.

There were several reasons for that skepticism. Once people started finding sex differences in brain structures in humans that were homologous to those found in animals, a distinction became obvious. The extent of sexual dimorphism in these brain regions was much smaller in humans than in other animals. For example, the SDNPOA is 5–6 times larger in volume in male rats than females (Gorski, Harlan, Jacobson, Shryne, & Southam, 1980). Yet in humans, depending on which hypothalamic nucleus you believe is homologous to the rat SDNPOA, you see at most a twofold difference between men and women (LeVay, 1991; Swaab & Fliers, 1985), and less than a threefold sex difference in rhesus monkeys (Byne, 1998). Likewise, the brain regions that control song are 5–6 times larger in males, who sing, than in females, who typically do not (Nottebohm & Arnold, 1976). We just never see sexual dimorphism of that degree in the human brain (Allen & Gorski, 1991). Or if you look at the spinal nucleus of the bulbocavernosus, where we see a threefold difference in the number of motor neurons in male rats versus female rats (Breedlove & Arnold, 1980), the homologue in humans, Onuf's nucleus, has a much more modest sex difference, as men have only about 50% more motor neurons than women (Forger & Breedlove, 1986).

To me, these findings that the nervous system was less sexually dimorphic in humans than other animals were a clue that hormones had lost much of their influence on the developing human nervous system. The relative independence from hormones would also fit with observations that humans are also less sexually dimorphic in physical appearance than other apes (Dixson, 2012). Also human conventions about sex differences in behavior, especially the extent to which some sex differences in behavior are displayed, have changed over the centuries. Those changes happened much too quickly for there to have been any fundamental change in the prenatal mechanisms of sexual differentiation. Rather, they had to be due to differences in culture and in socialization.

The basic hypotheses about development of human sex differences in behavior fall into two broad categories. One, that the same hormonal factors that masculinize the brain and behavior of other mammals are at work early in life in humans as well. The alternative is that social experience, and the differential treatments humans provide boys and girls (Golombok & Fivush, 1994), cause their brains to develop differently and for them to therefore behave differently, both during development and at adulthood. Babies are treated differently depending on their gender, as the Baby X experiments showed (Block, 1983). There is evidence that children display gender differences in behavior even before they seem to be aware of genders (Campbell, 2013; Martin & Ruble, 2010), so there may be some sex differences in behavior before social training has taken root. But it is still undeniable that children are exposed to the social role models of men and women and are encouraged, explicitly and implicitly, to behave like one particular gender. In the process of growing up, during that long slow process of neural development that typifies humans (Bogin, 1997), one can speculate that the brain is surely sculpted in a masculine or feminine fashion, including in terms of whether one would be attracted to the opposite sex or the same sex. Of course most social influences suggest that people should be heterosexual.

But if prenatal influences also affect sexual orientation, you can imagine a simple minded hypothesis that there is some threshold value of fetal androgen exposure such that individuals exposed to enough hormone will, when they grow up, be *gynephilic* (attracted to females). Conversely, individuals who are exposed to less than that threshold amount of androgen stimulation would grow up to be *androphilic* (attracted to males). This would explain why about 95% or so of men are attracted to women and about that proportion of women are attracted to men.

Notice that in trying to distinguish between these two hypotheses, heterosexuals are completely uninformative, because their outcome is equally compatible with both hypotheses, prenatal androgen or socialization. We do not know whether most people are straight because the women were not exposed to high testosterone before birth, while the males were, or because they have been socialized to be that way. What is interesting about gay men and lesbians is that they defy *both* of these hypotheses—they conform to neither the level of prenatal hormone exposure they were presumably exposed to nor the social expectations of how they should behave. To me this has always been an interesting puzzle, not because I think lesbians and gay men need to be explained (or changed!), but because *straight people* need to be explained. How can half of them think Brad Pitt is an ideal sexual partner when the other half finds him completely unacceptable? If we can understand why gays and lesbians defy both hypotheses about orientation, that might help us understand why most people are straight. If gay and lesbian orientations are found to be due to some variation in social influence, then that would argue that straight orientations are due to social influences. Conversely, if gay men and lesbians seem to receive the same social influences as everyone else, but are found to differ in terms of prenatal influences, that would argue that prenatal influences are likely to be a factor in the sexual orientation of straight people as well.

The Glass Half Empty

In weighing these two hypotheses, prenatal androgens versus social influence, for the orientation of straights and gay people, I was totally skeptical that there was any prenatal androgen influence at all, until 1998. Up until then, it seemed to me that most of my colleagues who study human behavior rather than animal models were looking at the same data that I was, and while I was very skeptical that they indicated any influence of prenatal androgens, other people seemed to find the same data persuasively supported the opposite view. One instance is the famous John/Joan case. I distinctly remember the first time I heard this story, my freshman year in college in Introductory Psychology. I was lucky to have the eminent developmental psychologist William Kessen as the instructor. He told us the story of monozygotic twin boys, one of whom was subjected to an accident during a circumcision that resulted in his penis being destroyed. Because of that, the family had been advised to raise that twin as a girl, while the other twin was being raised as a boy. What Kessen told us, relaying John Money's public lectures and published descriptions (Money & Ehrhardt, 1972), was that the girl was now a teenager who was perfectly happy in a female role while her brother was perfectly happy in a male role. That story provided an important existence proof. If even a single individual exposed to normal male levels of androgen before birth and just after birth (which would have fully masculinized a rat's brain) could, under the influence of socialization as a female, grow up to be happy as a woman, then prenatal influences could not be very important.

We now know that Professor Kessen was badly misinformed, because in fact the child was very unhappy, eventually rebelling against being a girl and changing his gender role to that of a male (Diamond & Sigmundson, 1997). I found this out when my son's copy of Rolling Stone magazine arrived in the mail one day (Colap-

into, 1997). For some people in the field, this later revelation of the case was a great vindication of the idea that prenatal hormones are involved in human gender identity, that the child's desire to be a male was due to the hormones he was exposed to before birth. The idea was that his brain was masculinized before birth and therefore he was fated to take on a male gender role when he grew up, including being attracted to women, despite socialization as a girl (Colapinto, 2000). My reaction was quite different. First, I conceded that this case no longer provided an existence proof of the unimportance of prenatal androgen. But beyond that, it did not seem to me that this particular anecdote could prove *anything*. One problem with this case was the fact that the surgical accident did not happen until the baby was 7 months old, so up until that time presumably the child was socialized as a male. Also, when you look more carefully into what happened, that decision to socialize the individual as the female did not happen overnight—it was a process. Finally, and perhaps most importantly, I have to wonder the extent to which the family was able to successfully shift gears and change their attitudes toward this child, to consider their son to now be a daughter.

I was skeptical that this case showed any influence of prenatal testosterone on the brain, because there was surely incomplete or imperfect socialization of the child as a girl. Thus, we do not know whether this unfortunate child grew up to feel like a male because of prenatal testosterone or because of incomplete socialization as a female.

More convincing research with disorders of sexual development, namely of genetic males born with cloacal exstrophy who are raised from birth as females, would eventually come to light. Nearly all of those individuals would report being attracted to females, whether or not they identified as females themselves (Reiner, 2004; Reiner & Gearhart, 2004). Those findings fit well with my current views, as we will see, but were known only through rumor in 1998.

Another set of studies that some people found persuasively arguing for a role of prenatal hormones on sexual orientation were the reports of congenital adrenal hyperplasia (CAH), where adrenal glands that are unable produce glucocorticoids instead produce androgens as a spillover product before birth. A female fetus with this condition may be exposed to sufficient androgens to masculinize the genitalia, presenting an intersex phenotype at birth. These individuals upon reaching adulthood are more likely to be lesbians than are control girls (Meyer-Bahlburg, Dolezal, Baker, & New, 2008). For some people, the fact that these girls are more likely to be lesbian when they grow up, despite socialization as females, indicated that prenatal androgens indeed affect human sexual orientation.

But again, I was very skeptical of this interpretation. One reason is that while these girls are more likely to be lesbians than control girls, *most of them are straight*. In fact, if you look at the reports more closely, you see that most of these individuals are not having sex with anyone. If in fact you thought prenatal testosterone was important for inducing gynephilia, then you could ask why are not all the women with CAH, or at least most of them, lesbians? And as in the John/Joan case, it was always possible that the parents, upon seeing their babies' intersex phenotype, may have been confused about, or felt ambivalent about, their child's sex, and so may have inadvertently socialized the child in such a way that she was more likely to be a lesbian upon growing up.

Likewise, the fact that these girls were subjected to doctor's visits and especially if they received cosmetic surgery to change the appearance of genitalia, you have to wonder whether that process had any influence on the child's burgeoning sexual attitudes. Also, it always seemed to me that if in fact we think that sexual orientation is more fluid in women than in men (Diamond & Rosky, 2016), then these women may have been exercising an option of becoming lesbians for other reasons. The very fact that there was something anomalous or uncommon about their genitalia might make such girls more self-conscious and therefore more receptive upon growing up to choosing women as sexual partners, not because they were particularly gynephilic, but because they judged women to be more accepting of their atypical genitalia. If many of the women with CAH were not having sex with anyone, that also might be related to hesitations in becoming intimate. So I did not find the CAH literature at all convincing that there was any prenatal influence on human sexual orientation.

Likewise, the groundbreaking work in 1991 from Simon LeVay, showing that a brain structure in the hypothalamic region known as INAH3, known to display a sex difference (Allen, Hines, Shryne, & Gorski, 1989), also differed between gay and straight men (LeVay, 1991), while compelling evidence that sexual orientation is not just a superficial difference, did not address at all the question of how orientation developed during ontogeny (as LeVay himself made clear at the time). We cannot know whether the gay men were born with a small IN AH3 that caused them to develop a gay orientation, or some other process made them develop a gay orientation and, in doing so, caused INAH3 to be smaller than in straight men. I loved the report, and the tying of the animal literature to the human brain, but it did not do anything to dissuade my skepticism about prenatal androgens affecting the human brain. Later studies in sheep would reveal that the homologous brain region is larger in rams that prefer to mount ewes than in rams that will mount only other rams (Roselli, Larkin, Resko, Stellflug, & Stormshak, 2004). But in 1998, those findings were still in the future.

Retrospective Markers of Prenatal Androgen Exposure

Until that time, all the data regarding whether there is any influence of prenatal hormones on human sexual orientation seemed completely, beautifully ambiguous to me, because in all the cases there was ample room for social influences to have actually played a role in guiding development of sexual orientation, rather

than the influence of prenatal hormones per se. But then Dennis McFadden published a report of a difference between lesbians and straight women that I could not explain away as a result of socialization. This was the report that click-evoked otoacoustic emissions, which are less frequent in males than females, a sex difference that is present at birth, are also less frequent in lesbians than straight women, with bisexual women intermediate between the two (McFadden & Pasanen, 1998). What I found compelling about this report was the very fact that these otoacoustic emissions were *cryptic*, out of sight and out of mind, as virtually no one among the public knew they even exist. I could not see any way that parents or teachers or peers or the individuals themselves could have noticed any difference in the future lesbians' otoacoustic emissions compared to other girls. These data upset my expectations, and would be replicated when McFadden examined other sexually dimorphic aspects of the auditory system, including spontaneous otoacoustic emissions (McFadden & Pasanen, 1999) and auditory evoked potentials (McFadden & Champlin, 2000).

Perhaps that made me more open-minded to the influence of prenatal androgens on human sexual orientation when I learned a year later about a sex difference in the pattern of finger lengths in humans. I was very familiar with the literature about sexual differentiation in the body of mammals, including humans, but I had never heard of this sex difference. When I read that the sex difference in the pattern of digit lengths was present in 2-year-old children (Manning, Scutt, Wilson, & Lewis-Jones, 1998), it seemed quite likely to me that the difference was the result of sex differences in prenatal exposure to androgens, a guess that was well vindicated by later studies. Those would include finding that the ratios are masculinized in people with CAH (Brown, Hines, Fane, & Breedlove, 2002c), are feminine in XY women with androgen insensitivity (Berenbaum, Bryk, Nowak, Quigley, & Moffat, 2009), and are exquisitely sensitive to prenatal hormone manipulations in mice (Zheng & Cohn, 2011).

The sex difference in the pattern of finger lengths is that the ratio of the length of the second digit divided by the length of the fourth digit, the so-called 2D:4D ratio, tends to be smaller in men than in women. This is not a big difference—if it had been, Aristotle would have told us about it. The sex difference has a d' of about 0.5, which Cohen would call a medium effect (Cohen, 1988). Cohen offers a terrific analogy that such a difference is roughly equivalent to the difference in height between 14- and 18-year-old girls. We all know plenty of 14-year-old girls who are taller than plenty of 18-year-old girls. In other words, there is a lot of overlap. If I were to show you 20 girls and tell you that ten are 14 years old and ten are 18, you would not be able to classify them accurately based on height alone. On the other hand, if I were to sort them by age and tell you the average height of each of the two groups, you would almost always be correct selecting the group with the taller average height as the 18-year-olds (if they were random samples of girls from each age group). So if we are going to use these digit ratios to look for any differences between groups we are going to have to use random sampling and gather large sample sizes because any differences between *subgroups* of a sex, such as gay versus straight men, or straight women versus lesbians, would presumably have d's even smaller than 0.5 because we expect sexual orientation differences to be smaller than sex differences.

We would later learn that digit ratios are also sexually dimorphic not just in 2-year-olds, but in fetal tissue (Galis, Ten Broek, Van Dongen, & Wijnaendts, 2010; Malas, Dogan, Evcil, & Desdicioglu, 2006), so the sex difference cannot be the result of socialization. Instead, the sex difference is almost certainly the result of differences in prenatal hormone exposure. For example, women with androgen insensitivity syndrome (AIS) have feminine digit ratios compared to control men (Berenbaum et al., 2009). This result tells us that the sex difference cannot be due to sex chromosomes acting directly on digit growth, nor can it be an effect of anti-Mullerian hormone (AMH) from the testes, since like men, these women have XY genotypes and developed testes secreting AMH before birth (which is why they lack Mullerian duct structures like a uterus and oviducts). As the only mechanisms for sexual differentiation of the human body that have been identified to date are social influences, sex chromosomes, AMH, or androgens, then having eliminated the first three mechanisms for engendering the sex difference in digit ratios, the last remaining candidate is prenatal testosterone.

An early indication that digit ratios are indeed due to prenatal androgen was the report that people with CAH, who are exposed to greater androgen levels before birth than same-sex controls (Wudy, Dorr, Solleder, Djalali, & Homoki, 1999), have smaller, i.e., more masculine, digit ratios than controls (Brown et al., 2002c). We reported this in 2002 and so did another group that same year (Okten, Kalyoncu, & Yaris, 2002). The same sex difference in 2D:4D ratios (female > male) are present in mice (Brown, Finn, & Breedlove, 2002a). Later, hormone treatments coupled with genetic manipulations in mice made it clear that androgens act upon androgen receptors in the paw itself to promote the growth of the fourth digit more than the others (Zheng & Cohn, 2011). These reports indicate that sex differences in digit ratios are indeed due to differences in prenatal exposure to androgens.

There are several advantages to digit ratios as markers of prenatal androgen. One is that no one knows about them, or at least no one knew about them in 1999. So we do not have to worry that any boys or girls out there were looking at their hands and thinking, "gee my hands are different than those of other people of my sex, maybe I am different." The other great aspect of digit ratios is that they are easy to obtain, and if you xerox them, they are easy to measure blindly, i.e., the person doing the measurement has no idea whether this particular person was male or female, gay or straight. There are plenty of disadvantages, of course, the biggest being that digit ratios offer a far from perfect correlation with prenatal androgens. In other words, they are noisy. On the other hand, we know how to exploit noisy markers to find differences between groups by

using statistics (like determining whether 18-year-old girls are taller than 14-year-old girls).

So we asked whether digit ratios vary by sexual orientation within a sex. When I began this study, I was a complete skeptic. I did not think we would see any differences at all and I did not really have any predictions about whether we would be more likely to see differences between gay and straight men, or between gay and straight women. But what we found was quite clear-cut. First we found, as others had before and since, that the sex difference is greater in the right hand than the left in both humans (Honekopp & Watson, 2010) and mice (Zheng & Cohn, 2011). In fact, in our sample we did not see a significant sex difference in digit ratios on the left hand, only on the right. We also found that the right-hand ratios of women who told us they were lesbians were significantly smaller than those of women who told us they were straight. Interestingly, we saw no difference between gay and straight men (Williams et al., 2000). The next year we replicated our study when we went back to a gay street fair in Oakland, again asking people about their sexual orientations but this time asking one more question—to tell us whether they considered themselves butch or femme. We did not define the terms, just asked them to choose one or the other. Of course, people were free to not answer any question, but we had a sufficiently large sample of women respondents that we saw, again only on the right hand, that lesbians who told us they considered themselves butch had more masculine digit ratios (smaller digit ratios) than those who told us they were femme (Brown, Finn, Cooke, & Breedlove, 2002b). This finding fits well with earlier reports that butch lesbians have higher levels of salivary testosterone than femme lesbians, and also recall more gender atypical behavior as children (Singh, Vidaurri, Zambarano, & Dabbs, 1999).

As with the earlier otoacoustic emission data, I could not think of any way to explain these differences in digit ratios between straight women and lesbians in terms of a social influence. But of course at the time, we also had to consider the possibility that we were unlucky, that the difference we saw was a fluke, a type I error, finding a difference between samples when in fact the populations they represent are not different. In other words, we may have had unrepresentative samples. But replications of our report began popping up right away (Csatho et al., 2003; Hall & Love, 2003; Kraemer et al., 2006; McFadden & Shubel, 2002; Putz, Gaulin, Sporter, & McBurney, 2004; Rahman, 2005; Rahman & Wilson, 2003; Tortorice, 2002; Wallien, Zucker, Steensma, & Cohen-Kettenis, 2008). I am certain that I will never again conduct a study that will be replicated as often this one. It has been replicated many times in many different laboratories, each time that the digit ratios of lesbians are smaller than those of straight women. A meta-analysis in 2010 concluded there would need to be 58 consecutive null findings before we should doubt whether there is in fact difference in the digit ratios of lesbians versus straight women (Grimbos, Dawood, Burriss, Zucker, & Puts, 2010). To my mind among the most compelling of these replications are the two with the smallest sample sizes. Hall and Love (2003), examining just seven pairs of monozygotic twins who were discordant for sexual orientation, found that the lesbian twins, on average, had more masculine digit ratios than the straight twins. This finding was replicated 9 years later in a Japanese study of eight pairs of twins (Hiraishi, Sasaki, Shikishima, & Ando, 2012), which was published after the 2010 meta-analysis. In the midst of a so-called replication crisis in psychology (Maxwell, Lau, & Howard, 2015) as well as life sciences and physical sciences (Baker, 2016), it is noteworthy that so many different laboratories have found this difference between lesbians and straight women.

Thus, I feel completely confident in saying that there is a sex difference in the average digit ratios of lesbians versus straight women. I have a pretty good imagination, but I can think of no way to explain that difference except to say that lesbians, on average, were exposed to more prenatal androgen than were straight women. And I do not know how to understand that conclusion, except to say that girls who are exposed to greater androgens before birth are more likely, when they grow up, to be lesbians. The other thing that is reassuring about the digit ratio findings is that they fit with the data from otoacoustic emissions, where once again there was difference between lesbians and straight women, but no difference between gay and straight men. Of course, both sets of findings using these two markers of prenatal androgens are consistent with the findings about the John/Joan case, women with CAH, and the reports of gynephilia among XY males with cloacal exstrophy who were assigned a female role at birth (Reiner, 2004; Reiner & Gearhart, 2004).

An important caveat about these findings is that although the difference between groups has been confirmed many times, this does not mean that you can use digit ratios make any accurate prediction about the sexual orientation of an *individual*. Because there is sufficient noise in the data, finger length ratios do not represent a shibboleth, a way to distinguish a lesbian from a straight woman, or even a man from a woman, with any degree of accuracy. On the other hand, given that greater prenatal androgen exposure makes females more likely to develop gynephilia, then probably the reason 95% of males develop gynephilia is because they were all exposed to even more prenatal androgens than any future lesbian. So why do any males grow up to be gay?

No Evidence of Under-Androgenization of Gay Men

It seems to me that in the field there is an expectation that gay men were exposed to less androgen before birth, that their androphilia is the result of hypo-androgenization before birth. But the fact that there is no difference between gay and straight men in digit ratios (Grimbos et al., 2010) or otoacoustic emissions (McFadden & Pasanen, 1998), tells me that, in defiance of those expectations, variance in prenatal testosterone cannot explain variance in human sexual orientation among men.

We can see in the old literature hints to explain why this might be the case. In terms of hormonal influences on behavior, the

amount of androgen in circulation in males is more than enough to have a maximal effect on behavior. In the classic demonstration, individual differences in the vigor of mating behavior across male guinea pigs cannot be due to individual differences in androgen. If you take those male animals that are either high or low or medium copulators, then castrate them, they all eventually stop mating, as Aristotle would have predicted. Crucially, if you now give all the male guinea pigs the exact same amount of testosterone, mating behavior returns, but they once again segregate into those same groups of high, medium, and low copulators (Grunt & Young, 1953). So variance in copulatory behavior across male guinea pigs is not a function of variance in circulating testosterone. Later studies would show that in fact, providing one-tenth as much testosterone as is normally in circulation to castrated male rats will completely maintain copulatory behavior at the levels that they were showing before castration (Damassa, Smith, Tennent, & Davidson, 1977). This is why, when male rats are screened to find those that will reliably copulate (studs) and those that will not (duds), there are no significant differences in their circulating levels of androgens. Rather, there must be differences in how their brains respond to those perfectly adequate levels of androgens (Clark, Davis, & Roy, 1985).

Thus, we say testosterone has a *permissive* effect on male sexual behavior. There has to be some testosterone on board in order for the individual to show any male copulatory behavior. But beyond that very low threshold amount (e.g., a tenth of normal male levels in rats [Damassa et al., 1977] which is well within the normal female range), any additional testosterone does not explain variance in the extent of the behavior. Testosterone permits the behavior to be displayed, but does not explain variance in that behavior. By analogy, probably every male human got all the fetal androgen exposure needed to do whatever androgens might do to favor gynephilia. By elimination, maybe they differed in terms of their response to that androgen.

What is the source of variance between gay and straight men? If you look at the data, you can conclude that it is not due to differences in prenatal testosterone. Indeed, penile size should be a more sensitive measure of prenatal androgen exposure than digit ratios or otoacoustic emissions, yet gay men have larger penis measures than straight men (Bogaert & Hershberger, 1999; Nedoma & Freund, 1961), which does not fit the idea that they were under-androgenized. The behavior of gay and straight males also suggests that a simple difference in overall masculinization could not be explained by differences in androgenization. For some sex differences in behavior, such as mental rotation, or math reasoning, or rough and tumble play, gay men tend to be less masculine, on average, than straight men (e.g., LeVay, 2016; Lippa, 2008; Rieger, Linsenmeier, Gygax, & Bailey, 2008). But on the other hand, these behaviors display either modest or small sex differences. The compelling sex differences in human behavior are those that have to do with sexual attitudes. In terms of interest in casual sex, attraction to older partners, concern for partner's attractiveness, frequency of masturbation, interest in visual pornography, in all those behaviors gay men are just as masculine as straight men. If you really think there was a global difference between them in terms of prenatal testosterone, how would you explain that they are so masculine, maybe even hypermasculine (e.g., for masturbation; Gerressu, Mercer, Graham, Wellings, & Johnson, 2008), in terms of those behaviors that show the greatest sex differences among straight people?

If we listen to the data, we have to conclude that the variance in sexual orientation in men is not due to variance from prenatal *exposure* to testosterone, so by elimination it must be due to variance in individual *response* to prenatal testosterone. In terms of thinking of hormonal effects, if there is any influence of prenatal testosterone on human behavior, we know that it is acting through the androgen receptor not through the estrogen receptor, since men with a dysfunctional gene for aromatase (and therefore a profound deficiency of estrogen) are nevertheless gynephilic (Morishima, Grumbach, Simpson, Fisher, & Qin, 1995). We also know that there is only one androgen receptor because of the effects of androgen receptor insensitivity on phenotype (i.e., a mutation in that single gene is enough to block all androgen-mediated masculinization of the body [Prior et al., 1992] and, apparently the brain, since women with AIS, whose estrogen receptors are intact, report they are androphilic [Money & Ehrhardt, 1972; Money, Schwartz, & Lewis, 1984]). Whether they are going to be gay or straight, all males are getting plenty of testosterone, which means they are all getting plenty of stimulation of the androgen receptor.

Thus, the difference would be in terms of which genes are being regulated by the androgen receptor—processes downstream from the binding of hormone to the androgen receptor. In other words, how genes are regulated when the androgen/receptor complex interacts with DNA. An important concept is that different sets of genes are being influenced by the activated androgen receptor in different tissues. One set of genes are important for responding to the androgen receptor to influence digit growth, other genes are responding to affect growth of genitalia (although we know there is some overlap in those sets of genes, specifically the HoxA genes [Dickman, 1997]), and yet other genes are probably being driven by androgen receptor to contribute to sex differences in the brain, and we have no idea what those genes are. Presumably they also influence orientation. They cannot all be the same sets of genes responding to the androgen receptor because if that were the case, there would never be any variance between men in orientation. But beyond predicting that the androgen-responsive genes that favor gynephilia will have an androgen response element somewhere upstream and will be expressed primarily, perhaps exclusively, in the brain, I can offer no further guidance to those studying genetic influences on sexual orientation (Hamer, Hu, Magnuson, Hu, & Pattatucci, 1993; Mustanski, Chivers, & Bailey, 2002; Sanders et al., 2015).

But we do know of another prenatal influence that affects sexual orientation in men—the fraternal birth order effect (Blanchard, 1997). This does not seem to be a socially mediated effect, since older step-brothers have no effect and older brother

raised apart do (Bogaert, 2006). Furthermore, it seems to apply only to males who are consistently right-handed (Blanchard, Cantor, Bogaert, Breedlove, & Ellis, 2006), which would seem to rule out any socially mediated effect unless one posits that older brothers somehow interact differently with younger brothers who are right-handed versus left-handed. In any case, these findings readily conform to the general findings that human sexual orientation does not seem to be a matter of what laymen think of as "choice," which is in fact a very difficult concept to even evaluate empirically (Bailey et al., 2016).

While confirming that prenatal events play a role in sexual orientation in both women and men, these findings do not conform with certain expectations in the field. First, it is well established that sexual orientation in women is in some sense "fluid" or at least more fluid than in men (Diamond, 2008a). Likewise, the "femme" lesbians in Brown et al. (2002b) presumably were not exposed to elevated prenatal androgens and reached their orientation through some other path. Such findings are sometimes taken to demonstrate that lesbians and straight women are not natural "kinds" of women, that is, they do not represent separate types of individuals. Indeed, it seems very likely that in samples comparing lesbians and straight women, at least some of the women in the lesbian sample had been straight during earlier periods of their lives and probably did not differ from women in the straight sample in terms of prenatal androgen exposure. Interestingly, femme lesbians appear to be more fluid in their orientation than butch lesbians (Diamond, 2008b), perhaps because they were exposed to too little prenatal androgen to influence orientation. The presence of these women in any lesbian sample should make it more difficult to detect any difference in prenatal androgen between them and straight women, and yet differences in digit ratios have been found repeatedly (Grimbos et al., 2010). So despite the fluidity of sexual orientation in women, there is still compelling evidence that prenatal influences matter, too, and that is an argument in support of the notion that straight women and lesbians do represent different kinds. To avoid misunderstanding, note that saying there are different kinds of people does not in any way mean that one kind is "lesser than" another, as the issue of sex differences has, I hope, taught us.

Similarly, the fraternal birth order effect on male sexual orientation suggests, at least to me, that gay and straight men are different kinds of people because when samples of each are gathered, the gay men consistently have an overrepresentation of brothers among their older siblings and the straight men do not (Blanchard & Bogaert, 1996; Blanchard et al., 2006; Blanchard, Zucker, Siegelman, Dickey, & Klassen, 1998). If there is no polarity of sexual orientation among men, how could we explain this consistent difference between samples of men classified simply as gay or straight? Of course, having made this point that there are objective, replicated differences in prenatal influences between gay and straight samples of both men and women, does not mean that there is no continuum of sexual orientation, that it exists only as a binary. Clearly there is a continuum of sexual orientation, as the Kinsey scale implied. All I am saying is that there must be *some* polarity of sexual orientation, otherwise simply sorting people into just these two categories should not reveal consistent differences in their developmental histories. The data do not fit the expectation that we are all distributed in some equal measure across each gradation.

As for the differences between gay and straight men, there is no evidence that they were exposed to different levels of prenatal androgen. In fact, I think the data strongly argue that they were *not* exposed to different levels of prenatal androgen. The data do not fit the expectation. Perhaps it is time to abandon the idea that gay men are under-masculinized and instead pursue alternative ideas about how they came to deflect the influences of both prenatal androgens and a heterosexist culture. Understanding that puzzle might help explain why straight people are, with no insult intended, so very common.

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Compliance with Ethical Standards

Conflict of interest The author declares no conflict of interest.

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