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# Biology of Human Gender, The 

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## Synonyms

Digit ratio; Femininity; Gender development; Masculinity; Prenatal androgens; Sex differences

## Definitions

The development of human gender identity may be influenced by organizational effects of prenatal hormones. This includes physical and neural development. Digit ratio (or 2D:4D) is a proxy of fetal hormones that correlates negatively with prenatal testosterone and positively with prenatal estrogen. Studies investigating associations between 2D:4D and sex-dependent traits suggest
that in addition to genetics, prenatal hormones contribute to the determination of gender.

## Introduction

At birth, humans are typically assigned to their biological sex (male or female) on the basis of their genitalia. But there is evidence from fetal studies that the sexual differentiation of the body occurs before the sexual differentiation of the brain (Swaab 2007; Bao and Swaab 2011). This gives the opportunity for considerable plasticity with regard to the social roles that are considered appropriate for males and females. These roles vary across societies such that it is appropriate to refer to the sexes as "male" and "female," but to their culturally influenced gender roles as "masculine" and "feminine." Here, we address the problem of the biological core of gender roles. Does it exist, and if so how important is it in influencing behaviors that we consider to be "masculine" and "feminine"? These questions are important in both a Darwinian and a socialcultural context. Our direct fitness is measured in number of offspring. It is in part dependent on the function of our gonads. However, if there is a mismatch between gonadal development and the sexual differentiation of the brain, then the result may be a reduction in fitness. Such transgendered individuals may be fairly common. In a large ( $n>255,000$ ) online study (The BBC internet study; Reimers 2007), $47.3 \%$ of participants
gave their gender as female and $52.7 \%$ as male. In answer to the question "Regardless of your biological sex, what sex do you feel?", a total of $4.0 \%$ of "males" selected "female" and $4.3 \%$ of "females" selected "male." Clearly, there may be both sociocultural and biological factors at work here. We briefly consider the former before discussing the latter in more detail.

## Gender and Social Influences

One influential model regarding the social etiology of gender is the gender schema theory (Bem 1981). This envisages gender-associated information is transmitted by schemata or networks of information. Bem maintained that there are individual differences in the degree to which people hold these gender schemata. These differences can be seen by the degree to which individuals are sex-typed.

Another important theory which considers social factors in the determination of gender is that of social role theory (Eagly 1997). This suggests that the labor division between men and women is a major determinant of gender differences. Thus, men and women are expected to fulfill different roles in the work force and then assumed to exemplify the characteristics of those roles. Work force roles are strongly related to interest in things (stronger in men) and in people (stronger in women) and these preferences are remarkably robust across cultures (Lippa 1998). Such patterns could be construed to support both a social and a biological influence on gender.

The concepts of masculinity and femininity and their marked plasticity can also be applied to societies (Hofstede 1991). Thus, a society can be called masculine when emotional gender roles are distinct. Men are assumed to be tough and preoccupied by material success and women are supposed to be tender and concerned with the quality of life. In contrast, a feminine society is one in which the emotional roles overlap such that both men and women are tender and concerned with the quality of life. The Masculinity Index (MAS) is a society-measure of preference for achievement, heroism, assertiveness, and material
rewards for success - independent of economic development. Countries such as Slovakia (MAS $=110$ ), Japan $($ MAS $=95)$, and Hungary $($ MAS $=88)$ have high masculinity scores, while Sweden (MAS $=8$ ), Norway (MAS $=8$ ), and the Netherlands (MAS $=14$ ) lie at the opposite end of the masculinity spectrum (Hofstede 1991). It is to be emphasized that MAS scores are independent of economic indices such as gross domestic product. Clearly, there are factors other than national wealth at work here.

## Gender and Biology

The plasticity of gender patterns is remarkable. However, this does not preclude a substantial biological effect on gender. Swaab and colleagues (Bao and Swaab 2011; Swaab 2004, 2007; Swaab and Garcia-Falgueras 2009) have discussed the interdependent biological processes involved in the formation of the reproductive system and in the subsequent sexual differentiation of the brain. In boys, the penis, prostate, and scrotum are formed during fetal weeks $6-12$. This begins under the influence of the Y-linked SRY gene (Berta et al. 1990) and continues with the production of testosterone and dihydrotestosterone. In girls, the development of the sexual organs primarily depends on an absence of large amounts of androgen. The masculinization/feminization of the nervous system and behavior occurs later in gestation and results predominantly from the permanent "organizing" effects of testosterone in the second trimester of development. Brain areas that show sex differences that relate to gender include the bed nucleus of the stria terminalis, the third interstitial nucleus of the anterior hypothalamus, and the shape of the corpus callosum (Saraswat et al. 2015). At puberty, the brain circuits that have been organized prenatally are activated by sex steroids (hence the term activational effects). In addition to this large effect of prenatal androgen, there are also genetic and epigenetic influences on the sexual differentiation of the brain during the second trimester (McCarthy et al. 2009). Associated with the sexual differentiation of the brain are medical conditions that are more common in
females (e.g., anorexia nervosa, bulimia, and Alzheimer's disease) or in males (autism, attention-deficit hyperactivity disorder [ADHD], and stuttering).

Prenatal androgens, such as testosterone, have also been implicated in the etiology of transgender identity. Transgender individuals have a gender identity that differs from their assigned sex, and in this regard, there is a preponderance of males over females (Bao and Swaab 2011). Some transgender individuals seek medical intervention to transition from one sex to another and are referred to as transsexuals. As with transgender individuals, male-to-female transsexuals (MTF) are more common than female-to-male (FTM) transsexuals (Bao and Swaab 2011). Transgender identity is not related in any substantial way to sexual orientation, suggesting different etiological pathways (Pauly 1998). Twin studies have provided evidence of a strong genetic influence on transgender identity (e.g., Heylens et al. 2012), and there are a number of studies indicating MTF individuals show atypical cerebral networks in both gray and white matter structures (reviewed by Saraswat et al. 2015). Overall, the characteristics of transgender individuals suggest a behavioral trait that is fixed early in development and is not substantially influenced by social factors.

The more nuanced effects of prenatal androgens on gender may be seen in studies using morphological proxies of fetal hormones and in assays of fetal hormones. With regard to morphological proxies, digit ratio (2D:4D) - the relative lengths of the second and fourth digits - is the most commonly used trait. The 2D:4D ratio is influenced by a balance of fetal testosterone to estrogen such that 4D length is increased relative to 2 D length when prenatal testosterone concentration is high relative to prenatal estrogen. Therefore males, with their high levels of prenatal testosterone, have longer fourth digits relative to second than do females (male 2D:4D $<$ female 2D:4D: Manning et al. 2004). Much of the sexdependent variation in 2D:4D appears to be determined in a rather narrow window of development towards the end of the first trimester (Manning 2002; Szwed et al. 2017). With regard to fetal sex steroids, data have been obtained from hormonal
assays of routine amniocentesis tests performed during the second trimester of development (Baron-Cohen et al. 2004).

Digit ratio studies have reported many associations between 2D:4D and sex-dependent traits. They include links between low 2D:4D (high prenatal testosterone relative to estrogen) in autism (Manning et al. 2001) and ADHD (Martel et al. 2008), and high 2D:4D (low prenatal testosterone relative to estrogen) in schizophrenia (Qian et al. 2016). Studies of 2D:4D in transsexuals has yielded mixed results. In some reports MTF individuals have higher (more feminized) 2D:4D than normative male controls but no effect in FTM individuals (e.g., Schneider et al. 2006). In contrast, FTM transsexuals have been reported to have lower 2D:4D than controls, but no effect in MTF individuals (e.g., Wallien et al. 2008). These discrepancies may, at least in part, result from differences in measuring finger lengths (see Leinung and Wu 2017 for discussion).

With regard to social role theory, 2D:4D and other testosterone-dependent traits have been linked to the labor division between men and women. Manning et al. (2010) have reported data from the BBC Internet study, showing that the proportion of women (PW) across occupations is moderated by two morphological correlates of testosterone (2D:4D and height) and a systemizin-g-empathizing score [SQ-EQ] - a putative behavioral correlate of prenatal testosterone. Systemizing is the drive to analyze systems or construct systems while empathizing measures a person's ability to understand thoughts and feelings of others (Baron-Cohen et al. 2004). PW varied per occupation from $17 \%$ in engineering and research \& development to $94 \%$ for homemakers. Tall women with low 2D:4D and high SQ-EQ scores tended to be found in low PW (male-dominated) occupations. Focusing on individual occupational preferences in the BBC study, Manning et al. (2017) found that low (masculinized) 2D:4D was related to preferences in heterosexual men and women for "male-type" occupations such as car mechanic, builder, and carpenter. Thus, we can see that a proxy for high prenatal testosterone (relative to estrogen) may interact with the pressures postulated by social
role theory. The result may be that prenatally masculinized women are attracted to "maletype" occupations.

Mean 2D:4D and the magnitude of sex differences in 2D:4D vary across nations. Such variation may correlate with between-nation variation in gender-related traits. For example, high national 2D:4D has been shown to correlate with high national scores for uncertainty avoidance and neuroticism (Manning and Fink 2011). Interestingly, countries that show the smallest sex differences in national 2D:4D also have low scores for gender inequality (Manning et al. 2014). This finding may map on to the national Masculinity Index (MAS). Further work is necessary to clarify this relationship.

Studies of 2D:4D and gender-related traits may overlap with reports concerning prenatal sex hormones and behaviors such as autistic traits and "tomboy" play patterns. With regard to the former, children with autism tend to avoid eye contact. A tendency for high levels of eye contact is associated with low concentrations of fetal testosterone (Lutchmaya et al. 2002) and high 2D:4D (Saenz and Alexander 2013). With regard to the latter, high levels of "male-typical" play in boys and girls are related to high concentrations of fetal testosterone (Auyeung et al. 2009). "Tomboyism," a tendency for girls to play with boys and boy's toys, is also associated with low (masculinized) 2D:4D.

## Conclusion

Gender is highly variable across individuals and across societies. These patterns speak to the notion that factors such as occupational roles are the major determinants of gender. However, there is much evidence that prenatal influences of both genes and sex steroid hormones contribute to the determination of gender. Such biological influences provide the substrate upon which social factors are built upon. In that sense they may provide the key to what we perceive as gender.

## Cross-References

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- Digit Ratio <br> - Gender Development Theory <br> - Hormone Effects on Human Fetal Development <br> - Male and Female Development <br> - Sex Differences <br> - Sexual and Reproductive Development <br> - Sexual Orientation and Human Sexuality
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## References

Auyeung, B., Baron-Cohen, S., Ashwin, E., Knickmeyer, R., Taylor, K., Hackett, G., \& Hines, M. (2009). Fetal testosterone predicts sexually differentiated childhood behavior in girls and in boys. Psychological Science, 20, 144-148.
Bao, A. M., \& Swaab, D. F. (2011). Sexual differentiation of the human brain: Relation to gender identity, sexual orientation and neuropsychiatric disorders. Frontiers in Neuroendocrinology, 32, 214-226.
Baron-Cohen, S., Lutchmaya, S., \& Knickmeyer, R. (2004). Prenatal testosterone in mind. Cambridge, MA: MIT Press.
Bem, S. L. (1981). Gender schema theory: A cognitive account of sex typing. Psychological Review, 88, 354-364.
Berta, P., Hawkins, J. R., Sinclair, A. H., Taylor, A., Griffiths, B. L., Goodfellow, P. N., \& Fellous, M. (1990). Genetic evidence equating SRY and the testis-determining factor. Nature, 348, 448-450.
Eagly, A. H. (1997). Sex differences in social behavior: Comparing social role theory and evolutionary psychology. American Psychologist, 52, 1380-1383.
Heylens, G., De Cuypere, G., Zucker, K. J., Schelfaut, C., Elaut, E., Vanden Bosche, H., et al. (2012). Gender identity disorder in twins: A review of the case report literature. The Journal of Sexual Medicine, 9, 751-757.
Hofstede, G. (1991). Cultures and organizations: Software of the mind. New York: McGraw-Hill.
Leinung, M. D., \& Wu, C. (2017). The biologic basis of transgender identity: 2D:4D finger length ratios implicate a role for prenatal androgen activity. Endocrine Practice, 23, 669-671.
Lippa, R. (1998). Gender-related individual differences and the structure of vocational interests: The importance of the people-things dimension. Journal of Personality and Social Psychology, 74, 996-1009.

Lutchmaya, S., Baron-Cohen, S., \& Raggatt, P. (2002). Foetal testosterone and eye contact in 12-month-old human infants. Infant Behavior \& Development, 25, 327-335.
Manning, J. T. (2002). Digit ratio: A pointer to fertility, behavior and health. New Brunswick: Rutgers University Press.
Manning, J. T., \& Fink, B. (2011). Digit ratio (2D:4D) and aggregate personality scores across nations: Data from the BBC internet study. Personality and Individual Differences, 51, 387-391.
Manning, J. T., Baron-Cohen, S., Wheelwright, S., \& Sanders, G. (2001). The 2nd to 4th digit ratio and autism. Developmental Medicine and Child Neurology, 43, 160-164.
Manning, J. T., Stewart, A., Bundred, P. E., \& Trivers, R. L. (2004). Sex and ethnic differences in 2nd to 4th digit ratio in children. Early Human Development, 80, 161-168.
Manning, J. T., Reimers, S., Baron-Cohen, S., Wheelwright, S., \& Fink, B. (2010). Sexually dimorphic traits (digit ratio, body height, systemizing-empathizing scores) and gender segregation between occupations: Evidence from the BBC internet study. Personality and Individual Differences, 49, 511-515.
Manning, J. T., Fink, B., \& Trivers, R. (2014). Digit ratio (2D:4D) and gender inequalities across nations. Evolutionary Psychology, 12, 757-768.
Manning, J. T., Trivers, R., \& Fink, B. (2017). Is digit ratio (2D:4D) related to masculinity and femininity? Evidence from the BBC internet study. Evolutionary Psychological Science. https://doi.org/10.1007/s40806-017-0098-4.
Martel, M. M., Gobrogge, K. L., Breedlove, S. M., \& Nigg, J. T. (2008). Masculinized finger-length ratios of boys, but not girls, are associated with attention-deficit/ hyperactivity disorder. Behavioral Neuroscience, 122, 273-281.
McCarthy, M. M., Auger, A. P., Bale, T. L., De Vries, G. J., Dunn, G. A., Forger, N. G., et al. (2009). The epigenetics of sex differences in the brain. Journal of Neuroscience, 29, 12815-12823.

Pauly, I. B. (1998). Gender identity and sexual orientation. In D. Denny (Ed.), Current concepts in transgender identity. New York: Garland Publishers.
Qian, W., Huo, Z., Lu, H., Sheng, Y., Geng, Z., \& Ma, Z. (2016). Digit ratio (2D:4D) in a Chinese population with schizophrenia. Early Human Development, 98, 45-48.
Reimers, S. (2007). The BBC internet study: General methodology. Archives of Sexual Behavior, 36, 147-161.
Saenz, J., \& Alexander, G. M. (2013). Digit ratios (2D:4D), postnatal testosterone and eye contact in toddlers. Biological Psychology, 94, 106-108.
Saraswat, A., Weinand, J. D., \& Safer, J. D. (2015). Evidence supporting the biologic nature of gender identity. Endocrine Practice, 21, 199-203.
Schneider, H. J., Pickel, J., \& Stalla, G. K. (2006). Typical female 2nd-4th finger length (2D:4D) ratios in male-tofemale transsexuals-possible implications for prenatal androgen exposure. Psychoneuroendocrinology, 31, 265-269.
Swaab, D. F. (2004). The human hypothalamus. Basic and clinical aspects. Part II: Neuropathology of the hypothalamus and adjacent brain structures. In M. J. Aminoff, F. Boller, \& D. F. Swaab (Eds.), Handbook of clinical neurology. Amsterdam: Elsevier.
Swaab, D. F. (2007). Sexual differentiation of the brain and behavior. Best Practice \& Research. Clinical Endocrinology \& Metabolism, 21, 431-444.
Swaab, D. F., \& Garcia-Falgueras, A. (2009). Sexual differentiation of the human brain in relation to gender identity and sexual orientation. Functional Neurology, 24, 17-28.
Szwed, A., Kosinska, M., \& Manning, J. T. (2017). Digit ratio (2D:4D) and month of birth: A link to the solstitial-melatonin-testosterone effect. Early Human Development, 104, 23-26.
Wallien, M. S. C., Zucker, K. J., Steensma, T. D., \& CohenKettenis, P. T. (2008). 2D:4D finger-length ratios in children and adults with gender identity disorder. Hormones and Behavior, 54, 450-454.

