Information Brief

SEX, GENDER AND GENETICS

This information brief attempts to highlight what is currently known about sex and gender from social and scientific research. Sex and gender have core roles in how individuals see their identity and their place in society, as well as in how societies structure themselves. As such, the topic is a contentious one that carries significant weight. Different societies, communities or groups may have divergent views on the relations between the two "typical" sexes and genders, and on individuals who do not fit into these binaries. While pgEd does not aim to pass value judgment or prescribe how different individuals or communities should think about these topics, we hold a basic belief in the dignity and worth of all people and their rights to personal security and respect. As pgEd strives to provide a balanced and multidisciplinary perspective on these topics as much as possible, we encourage readers to recognize that this field is a work in progress. We do our best to indicate points which are still controversial amongst researchers, who may not always agree on the meaning and implications of the relevant discoveries.

Key points

- At a genetic level, sex in humans is primarily correlated with sex chromosomes – XX in "typical" females, XY in "typical" males – but a variety of genes on other chromosomes influence the development of sexual features.
- A small but significant portion of the population does not fit into the male-female binary sex categorization. These individuals are usually referred to as "intersex."
- One category of intersex conditions arises when individuals have an atypical number of sex chromosomes. These individuals can exhibit a wide range of physical, cognitive and reproductive characteristics.
- Another category of intersex conditions results from genetic variants that affect the development of the reproductive system. These individuals may have sexual features that are ambiguous or different from what are typically expected based on their sex chromosomes.
- The gender identity of intersex individuals often cannot be predicted from the "maleness" or "femaleness" of their sexual features, underscoring the complexity

of how gender (the behavioral and social dimensions of being a man, woman, both or neither) maps onto sex.

- Transgender individuals are those whose gender identity does not conform with the gender typically associated with their physical or chromosomal sex.
- Third gender or other non-binary gender identities have been recognized by different cultures around the world and throughout history.
- There is some preliminary, but still controversial, scientific research into the roles of genetic and environmental factors (including levels of sex hormone exposure in the womb) in shaping an individual's gender identity.

Useful terms

Gene – A basic functional unit of genetic information in our DNA.

Genetic test – A procedure that gives some information about the genetic make-up of an individual.

Genetic variant – One of several possible DNA sequences at a particular location in the genome.

Genome – An individual's full set of genetic information, including all their genes as well as other segments of DNA that may regulate when genes are turned on or off.

Chromosome – An individual piece or molecule of DNA in the genome. In humans, each cell typically has 23 pairs of chromosomes, one pair of which consists of the sex chromosomes (X and/or Y), and the other 22 pairs are known as autosomes.

Binary – Something that exists only in one of two mutually-exclusive states.

Sex – Classification of people into "male," "intersex" or "female" based on physical characteristics, including chromosomes, sex hormones, and reproductive organs.

Gonad – An organ in the body (e.g., testis or ovary) whose function is to produce gametes (i.e., reproductive cells, including sperm or egg) and sex hormones.

Androgen/estrogen – Two of the major sex hormones, or chemicals produced by the body to regulate the development of the reproductive organs and sexual features. Androgens are typically found at higher levels in males, and estrogens are typically higher in females. However, both types of hormones are typically present at some level in everyone.

Intersex – Individuals whose sex does not fit into a male-female binary.

Gender – Behavioral, social and other aspects of the meaning or role in society of being a "man," a "woman," both, or neither.

Gender identity – A person's internal and individual experience of gender, which may or may not be the gender typically associated with their sex assigned at birth.

Gender fluidity – Having a gender identity that is not fixed and may shift between and among many genders.

Gender expression – A person's public presentation of their gender (e.g., masculine, androgynous, feminine), which may or may not reflect their gender identity.

Transgender – Individuals whose gender identity differs from the gender typically associated with their physical or chromosomal sex. Cisgender refers to individuals whose gender identity is the same as the gender typically associated with their physical or chromosomal sex.

Non-binary – General term for those gender identities that do not fit a man-woman binary.

Introduction

The division of the human population into two halves – men and women – seems at first glance to be one of the most obvious and natural distinctions in our species. However, recent decades of research in the biological and social sciences have shown that sex and gender in humans is a lot more complicated. While "sex" and "gender" have often been used interchangeably, they actually describe two distinct, but related, aspects of human identity. Moreover, sex and gender do not exist as simple binaries. From the DNA in our cells, to physiology, to behavior and societal roles, sex and gender exist as spectra that show gradients of differences across many dimensions. A more comprehensive and nuanced look at human history and culture also shows that, across different societies, sex and gender have often been viewed differently than in Western society today.

A genetics perspective of sex

At a genetic level, "sex" in humans – the physical and reproductive differences between "males" and "females" – is primarily correlated with the sex chromosomes. In "typical" females, the genome of each cell contains two X chromosomes, while in "typical" males, there is one X and one Y chromosome. A number of genes, on the sex chromosome and on the other non-sex chromosomes (called "autosomes"), play important roles in forming the testes and the ovaries – the reproductive organs, or gonads, where the reproductive cells (sperm and egg) mature. Some of these genes actively suppress the development of the testes and promote the development of the ovaries; conversely, other genes do the opposite, promoting ovarian development and suppressing that of the testes. In particular, one gene on the Y chromosome, SRY, is pivotal in directing the formation of the testes. The gonads also produce sex hormones that control the maturation of the reproductive cells as well as development of the sexual features of the body. Sex hormones include androgens (such as testosterone), which are typically present at higher levels in males, and estrogens, typically higher in females. However, both types of hormones are typically present at some levels in the bodies of all people.

Intersex and the sexual spectrum: How sex is not binary

While "typical" males and females have obvious physical and chromosomal differences, there is a small but significant portion of the population whose sex does not fit into this simple binary. These individuals are often referred to as "intersex." Some studies estimate that almost 2% of all people are intersex, which is roughly the same number of people who have green eyes or red hair.

Broadly, there are two categories of biological bases for intersex conditions. The first involves having an atypical number of sex chromosomes, e.g., XO (Turner syndrome; the O denotes the absence of a second sex chromosome), XXY (Klinefelter syndrome), XYY (Jacobs syndrome) or XXX (Triple X syndrome). It is also possible for some groups of cells in the developing fetus to lose one of the sex chromosomes, resulting in an individual who is a genetic "mosaic", with some cells that are XY (or XX) and others that are XO. Overall, these conditions are fairly common: Turner syndrome occurs in 1-in-2,500 people, and Klinefelter syndrome occurs in around 1-in-500 to 1-in-1,000 people. Individuals with atypical numbers of sex chromosomes have a wide range of physical, cognitive and reproductive characteristics.

The other main category of intersex conditions includes individuals who have typical combinations of sex chromosomes but possess other genetic variants that affect how the reproductive system develops. As of 2019, more than two dozen such genes have been identified (including situations where the SRY gene has moved from the Y chromosome to the X). Individuals with these conditions often have gonads that are nonfunctional (called "streak gonads") or, in very rare cases, have both testicular and ovarian tissues (called an "ovotestis"). At the same time, their external sex organs and secondary sexual features may take a range of forms — typical for what might be expected from their sex chromosomes, opposite of what might be expected, or ambiguous. Two of the most common groups of such conditions, which affect how the body produces or responds to sex hormones, are androgen insensitivity syndrome (AIS) and congenital adrenal hyperplasia (CAH). In AIS, genetic variants in the androgen receptor gene (which is located on the X chromosome) affects the body's ability to respond to androgens, leading XY individuals to have less-developed male features than typical males (even if they may have high levels of testosterone circulating in their bloodstream). In cases of complete AIS (CAIS), the person would have female sex organs and sexual features, but internal testes in place of ovaries. Conversely, in the majority of cases of CAH, genetic variants cause increased production of androgens which, in XX individuals, can lead to the development of typically male sexual features to varying degrees.

Together, these variations in sexual development create a spectrum that ranges from "typical" males, through intersex individuals, to "typical" females. Intersex babies that are born with distinctive physical features such as ambiguous genitalia may be

identified at birth. Others (including many individuals with CAIS) may not be identified until puberty or even later in life, often after experiencing fertility issues. Infants with ambiguous genitalia may be subjected, sometimes controversially, to surgical treatments intended to "masculinize" or "feminize" the baby. Some countries and intergovernmental bodies, such as the Council of Europe and the United Nations, have begun recognizing the rights of intersex individuals to not be subjected to such interventions without their consent.

Because certain hereditary diseases are determined by the sex chromosomes, genetic tests could play a role in the health management of intersex individuals. The growing popularity of direct-to-consumer genetic tests has also led to individuals discovering that their complement of chromosomes does not match their outward physical sex. At the same time, the advent of prenatal genetic tests (such as preimplantation genetic diagnosis of embryos or non-invasive prenatal testing) means it is now possible to genetically identify intersex individuals before birth. This has led to concern among members of intersex communities that the preferential selection against, or termination of, intersex embryos/fetuses might lead to increased stigma against their communities.

Sex and gender do not map neatly onto each other

Compared to sex, gender refers to the behavioral, social and other aspects of the meaning or role of being a "man" or "woman" in society. Many scholars, researchers, cultures and societies recognize that gender also exists as a spectrum. Individuals whose gender identity does not conform to the gender typically associated with their physical or chromosomal sex may identify themselves as *transgender*, or simply *trans* (as compared to *cisgender* individuals, whose gender conforms with their assigned sex). To live as a gender different from the one assigned at birth, some transgender individuals may desire to, are undergoing or have undergone hormone treatment and/or gender affirming surgery to transition socially and/or physically. In addition, while some trans people identify as trans men (men who were assigned female sex at birth) or trans women (women who were assigned male sex at birth), others identify as neither men nor women, a mix of both, or fluid/variable. These individuals are broadly described as *non-binary* or *genderqueer* (note that the language for talking about the diversity of human sex and gender continues to evolve, and not everyone in these communities identify with all, or any, of the terms used in this paragraph). Estimates for the prevalence of trans people in the population vary widely, partly due to the stigma often associated with identifying as trans, with figures between 0.5-1% being most commonly cited.

The gender identity of intersex individuals reinforces the complexity of how human gender relates to sex. Intersex people with biological features that do not match their chromosomal sex (such as XX individuals with CAH who have male features or XY individuals with CAIS who have female features) are more likely than the average

population to identify as a different gender than the one they are assigned to or raised as. At the same time, their gender identity often cannot be predicted from the "maleness" or "femaleness" of their sexual features.

While media attention on trans people has increased in recent years, particularly in the United States, the recognition of trans or non-binary people in society is not new. Throughout history and across different cultures, individuals with "third gender" (as well as "fourth gender" or even more varieties) have been recognized, with varying degrees of social acceptance. These include the *hijra* or *khawaja sira* of South Asia and the *kathoey* of Southeast Asia, who have been given legal recognition to various extents in countries such as India, Pakistan and Thailand. In addition, many Indigenous American peoples recognize individuals with third, fourth or otherwise non-binary gender roles, collectively referred to as "Two Spirit" people. It is important to note that the social and cultural meanings of these third/non-binary genders do not always correspond neatly with those of trans identity in Western societies, and there has been some concern in these countries or communities that Western transgender culture and identity may conflict with their traditional third gender culture.

Born this way?

People often wonder whether gender identity is primarily the result of biological/genetic or social/cultural factors - "nature vs. nurture." This question has been technically, logistically and ethically challenging to study, given the emotional and societally-stigmatizing nature of the topic, as well as the discrimination and threat faced by many LGBTQI+ (lesbian, gay, bisexual, trans, queer, intersex, and others) people throughout history. As such, this is a particularly controversial area of research. The results of these studies have often been inconsistent or contradictory, and usually suffer from small sample sizes and questions about how reliably or consistently gender is identified in the studies. For example, while some studies seem to show that the amount of androgen and/or estrogen that individuals are exposed to in the womb ("*in utero*") seem to have some effects on their gender identity, other studies have failed to bear out the results. At the same time, some neurological studies have examined the correlation between brain structure and gender identity. The results of some of these studies suggest that trans people have brain structures more similar to those of cisgender people who share their gender identity (so a trans woman would be more similar to a cis woman than a cis man). However, these results are complicated by the fact that brain structures can be the result, rather than cause, of behavior and life experience. Additionally, whether "male"/"female" brains are meaningfully different is itself controversial and inconclusive. Finally, studies of twins seem to suggest that genetic variation does, to a certain extent, affect gender identity, and a small number of regions in the genome are found to be associated with these traits. However, many such studies do not account for the fact that twins share the same *in utero* environment, and often experience the same or comparable environments when growing up. The bottom line is that, like all complex

human traits, gender identity is likely the result of the interactions of multiple genetic and environmental (including *in utero*) factors - "nature and nurture."

A more fundamental question is whether the rights and recognition of LGBTQI+ people should depend on their traits being inborn and immutable – "born this way." Some advocates and community members believe that finding an innate genetic or biological basis for their identities would help secure their fundamental rights. Others point out that even if identities are not inborn or innate, it doesn't mean they are "by choice." These individuals worry that an overemphasis on biological differences would trivialize the social and environmental influences on the development of our brains and identities and might simply create a biological basis for discrimination. This question is particularly relevant in light of research findings, as well as the lived experiences of individuals, that suggest gender and sexuality are often "fluid," shifting throughout one's lifetime.

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