GENES AND GENDER: WHY THEY NOT ALWAYS MATCH

Olga Oliveira Cunha¹, & Susana I. Sá²

¹Gabinete de Desenvolvimento Pessoal e Inclusão Social/NOVA FCSH (Portugal) ²Unidade de Anatomia, Faculdade de Medicina da Universidade do Porto (Portugal)

Abstract

Sexuality is considered an essential element of human nature, not only in its procreative aspect but also, and above all, as an affective manifestation of the establishment of relationships with another human being. In turn, the gender has been an important issue, particularly in the last thirty years since it has been linked mainly to the human rights. In the various declarations and plans approved at the different United Nations World Conferences, the evolution of this concept, and of others associated with it, has been raising questions with implications at the most diverse levels. These implications can be internal to each individual or in societal and cultural terms and in their organization, such as in the legal aspects, and, above all, in the way we think and experience the society in which we are inserted.

Sexuality, however, may also be considered as the inter-relation of gene and hormone systems that will determine the formation of genitalia, that will eventually imprint the neuronal systems where the affective manifestations take place. However, sometimes the genetic sexuality is not in conformity with the self-definition of gender. This discrepancy may be related with some neuronal systems related with the definition of self, in the construction of each own identity, and the relationship with other people.

If medicine has a saying in this matter, the psychoanalysis and psychoanalytic thinking have an essential role, which is paramount in promoting reflection on gender issues, whether in identity, or in the experience of sexuality as a whole. This reflection will allow the constitution of itself as a science that is not restricted to psychology, but that encompasses several areas of knowledge, allowing, through the free association method, to analyze and reflect on the essence of the human being.

In this presentation, these two issues will be addressed and confronted.

Keywords: Gender, genes, psychoanalysis, neurobiology.

1. Introduction

According to several authors, (Canella & Nowak, 1997; Moshman, 2014) development in human beings is a continuous process that begins with the act of conception. Two questions then arise: what happens and how it happens in human beings during their growth. It is defended and generally accepted that this process stems from various factors and internal influences, such as heredity and maturation; external influences, such as learning processes and environmental changes, as well as the interaction of both. This development is, generally and in most situations, regulated and proceeds through an invariable sequence which, despite being continuous, may not be gradual and smooth. We are aware of situations in which there were interferences in this process which resulted in permanent dysfunctions. What happens to sexual development is no different (Canella & Nowak, 1997; Moshman, 2014). Human sexuality experiences several changes during the life span, from birth to death, with varying intensity that can be considered unique in the various biological functions of the human being. In addition, in the society, we know, male and female sexual life cycles also differ in several significant respects.

2. Sexual dimorphism in the human beings

The truth is that most sex differences in human behavior or physiology are small or negligible, since, in terms of percentages, they are not that expressive (Hines, 2020; Joel, 2021). At the moment, science considers that human sexual dimorphism results from genetic (XX or XY chromosomes) and hormonal (release of androgens that bind to the respective receptors) conditions (Arnold, 2020; Grabowska, 2017; Pallayova, Brandeburova, & Tokarova, 2019).

The brain's sexual dimorphism is also dependent on behavioral and educational factors, as the way children are brought up and their preferences and playing skills; and social factors, as the way children integrate into society and how society defines their social roles (Hines, 2020; Khorashad et al., 2020). Both factors of great relevance for the psychological and psychoanalytic component. These two psychological characteristics are increasingly relevant and should be considered as modulators of neuronal morphology, since it has already been demonstrated that experience changes the morphology of the brain.

Likewise, biological characteristics are also considered as complementary and independent factors. Two initial moments affect sexual differentiation: on one hand, the expression of the Xist gene by the X chromosome that annuls the duplication of the expression of genes contained in the X chromosome in XX beings, eliminating the sexual differentiation of this expression; on the other hand the expression of the Sry gene by the Y chromosome that induces the formation of the male gonad, leading to the expression of testosterone and the Müllerian inhibitory hormone, inhibiting the formation of the female gonad (Arnold, 2020; Grabowska, 2017; Hines, 2020; Pallayova et al., 2019). However, mouse studies show that there are other phenotypic variations induced by the X and Y chromosomes; that is, the chromosomal expression of the gonad was separated by the somatic expression (by placing the sex genes in autosomes). These results showed the existence of different behaviors, even in animals with the same gonad, suggesting that there are sexually differentiated responses that do not depend on hormonal changes (Arnold, 2020). Genes expressed by the Y are mostly implicated in the formation of male-typical characteristics, which are regulated by testosterone sensitivity (Arnold, 2020; Hines, 2020; Raznahan et al., 2016). There are, however, external factors that may affect this regulation, namely endocrine disruptors or modulators (Azevedo, Martins, Lemos, & Rodrigues, 2014; Hines, 2020). However, there is sexual dimorphism prior to hormone production, often caused by epigenetic factors, which can reduce testosterone sensitivity in XY people and increase it in XX people (Marrocco, Einhorn, & McEwen, 2020; Rice, Friberg, & Gavrilets, 2016).

3. Homosexuality

These sexually dimorphic characteristics are mainly related to sexual behaviors and show certain reciprocity. So how is it possible for "sexual" relationships to exist with someone who belongs to the same biological sex?

Science has realized that human sexuality is very different from that of most of the lower animals in that it is not dichotomous. This difference is due more to psychosocial factors than to hormonal or brain organization (perinatal) factors.

The brain of homosexual people does not seem to differ from that of heterosexual people of the same gender. When the difference exists, it seems to be due to hormonal variations in the perinatal period (variations in testosterone levels), with, however, a great influence on the way children grows and interact with the environment and with others, which also ends up influencing their brain morphology (Bogaert & Skorska, 2020; Hines, 2020; Roselli, 2018).

What seems to be widely accepted is the fact that there are more differences between the brains of heterosexual men and women than between homosexual men and women. This is due to the fact that men's brains are very different between homosexuals and heterosexuals and explains the fact that non-heterosexual men are mostly homosexuals. Likewise, the biology of the brains of homo- or heterosexual women is not very different, consistent with the fact that most non-heterosexual women are bisexual, and their sexuality is more fluid (Bogaert & Skorska, 2020; Kagerer et al., 2011; Manzouri & Savic, 2018; Safron, Sylva, Klimaj, Rosenthal, & Bailey, 2020).

Anyway, and in general, the differences found in the brains of homosexual or heterosexual people are not generalized and the studies about the effects of hormonal variations during development did not prove to be correlated with differences in sexual orientation (Bogaert & Skorska, 2020; Dickenson, Diamond, King, Jenson, & Anderson, 2020; Kagerer et al., 2011; Khorashad et al., 2020). Therefore, there are other approaches in science that can help us understand these differences.

4. Gender dysphoria

However, if sexuality is something intrinsic and innate to human beings, and if it is, in fact, binary, how can gender dysphoria be explained? People with gender dysphoria, by definition, do not accept their gender condition. The vision they have of their bodies is not the one represented in their mental scheme. This situation usually brings a lot of anguish and unhappiness, because people cannot make their body representation a positive value (Chew et al., 2020; Jahanshad & Thompson, 2017; Schudson & Morgenroth, 2022). Dysphoria can reveal itself very early ("early onset"), appearing during

adolescence or before puberty, or later in adulthood (Bogaert & Skorska, 2020; Hines, 2020; Khorashad et al., 2020; Roselli, 2018).

Gender identities tend to be in line with the person's biological sex; however, they are not fixed structures. According to Stoller (2020) gender identity is "a mixture of masculinity and femininity in an individual, meaning that both masculinity and femininity are found in all people, but in different forms and degrees. This is not the same as the quality of being male or female, which has connotations with biology; gender identity begins with the perception of belonging to one sex and not another, being initially given through socialization, first by parents and later by friends, school, among others.

This begins before the age of 2 and continues into adulthood. It will result from five factors: a) the genetic biological factor (XX and XY chromosomes, referenced above); b) the recognition of the sex of the baby from the observation of the external genitalia; c) the influence of this morphological characteristic on the part played by the parents and the interpretation of these perceptions by the baby; d) the bio-psychic phenomena related to the above and e) the development of the body ego, resulting from the qualities and quantities of sensations, mainly in the genitals, which define the body and the psychic dimensions of the person's sex. Silva (1999) says, however, that Stoller is defining sexual rather than gender identity. Louro (1997) says: "It is observed that individuals can exercise their sexuality in different ways, they can "live their desires and bodily pleasures" in different ways. Their sexual identities are thus constituted through the ways in which they live their sexuality, with partners of the same sex, of the opposite sex, of both sexes or without partners [sexual orientations]. On the other hand, they also identify themselves, socially and historically, as male and female and thus build their gender identities. It becomes evident that these identities (sexual and gender) are deeply interrelated; language and practices very often confuse them, making it difficult to think them differently [...] What is important to consider here is that - both in the dynamics of gender and in the dynamics of sexuality - identities are always constructed" (Louro, 1997), p. 26-27).

But what is actually known about what happens in the brains of gender dysphoric and transgender people?

Science has not yet been able to show, unequivocally, differences in neuronal structure that justify gender dysphoria. The small inconsistencies detected are due to many variables that may not be taken into account in the studies and to small sample numbers (namely, if people are effectively dysphoric and/or if they are already undergoing hormone conversion therapy). Studies have shown that the morphology of the cortex is more related to genetic sex than to the dysphoric sex (the one that is felt). However, it has been shown that the neuroanatomical signature of transgenderism is related to neuronal areas that process information from the "being" and consciousness of your body (Burke, Manzouri, & Savic, 2017; Hines, 2020; Roselli, 2018).

While homosexuality is about sexual attraction, in gender identity the question is in the sex and gender representation with which the person identifies itself. More recent data seem to point to a disconnection between the frontal, occipital and parietal cortices, where the neuronal circuits that interconnect and process self-perception and body-perception are located (Buchanan et al., 2013; Burke et al., 2017; van Heesewijk et al., 2022).

More recent studies have shown that the effect of activating sex chromosome genes is independent and has almost as much weight in sexual differentiation as hormones. This knowledge can help shed light on some of the sociocultural and clinical considerations of the transgender person.

After all, the brain of men and women is not that different, and most of the differences it presents are the result of compensatory measures of the differences introduced by hormones during the physical and psychosocial development of the individual (Grabowska, 2017).

5. Conclusion

We can thus appreciate at least two conclusions. On the one hand, the experience, the education, and the psychology of each one are external factors that modulate neuronal biology from day one. Therefore, it is understood that no two people are alike, even homozygous twins, since they do not experience the same things, nor in the same way. On the other hand, biology, genes from parents passed on to children and the different activation of genes that predispose the individual to certain physiological, hormonal and behavioral responses, also affect living, education, and psychology.

Although the main lines of thought continue to formulate that the differences between men and women are dependent only on hormonal variations (testosterone levels) circulating during fetal development, many studies already point to a very relevant role in the activation of genes, either to increase the predisposition of neuronal (and other) systems to different concentrations of testosterone, or to display sexually different characteristics that can be inherited by offspring of the opposite sex. Therefore, the hypothesis that each one's experience can also promote neuronal differences that ultimately result from different orientations cannot be ruled out. Only then can we understand why individuals with the same hormonal inaccuracies' present different psychosocial responses (both in terms of sexual orientation and gender identity).

These inconsistencies in results and analyzes are mainly related to the fact that humans are the subject of the study. This is because: 1) people are very different, in order to have greater statistical power we need to study many people; 2) people's psychosocial profile is different and this greatly influences the results; 3) information about people's sexual orientation is dependent on the self-report, which may not correspond to the truth; 4) most reliable study and analysis techniques are invasive and unethical.

This type of incongruity also appears in transgender people. Some transgender people do not experience dysphoria; the definition of sexual orientation for transgender people is more complex; the hormonal treatments they undergo for gender transition increase (or introduce) the gender difference that might or might not exist.

There is still a long way to go in understanding the neurobiology of sexual orientation and gender identity. We think that as long as the biological sciences and psychology keep their distance, more time will take to be traversed.

References

- Arnold, A. P. (2020). Sexual differentiation of brain and other tissues: Five questions for the next 50 years. *Horm Behav*, 120, 104691. doi:10.1016/j.yhbeh.2020.104691
- Azevedo, T., Martins, T., Lemos, M. C., & Rodrigues, F. (2014). Hiperplasia congénita da suprarrenal não clássica – aspetos relevantes para a prática clínica. *Revista Portuguesa de Endocrinologia*, *Diabetes e Metabolismo*, 9(1), 59-64. doi:10.1016/j.rpedm.2013.12.001
- Bogaert, A. F., & Skorska, M. N. (2020). A short review of biological research on the development of sexual orientation. *Horm Behav*, 119, 104659. doi:10.1016/j.yhbeh.2019.104659
- Buchanan, B. G., Rossell, S. L., Maller, J. J., Toh, W. L., Brennan, S., & Castle, D. J. (2013). Brain connectivity in body dysmorphic disorder compared with controls: a diffusion tensor imaging study. *Psychol Med*, 43(12), 2513-2521. doi:10.1017/s0033291713000421
- Burke, S. M., Manzouri, A. H., & Savic, I. (2017). Structural connections in the brain in relation to gender identity and sexual orientation. *Sci Rep*, 7(1), 17954. doi:10.1038/s41598-017-17352-8
- Canella, P., & Nowak, L. (1997). Aspectos médicos da sexualidade. Silva, MC A.; Serapião, JJ; Jurberg, P.(orgs.) Sexologia: fundamentos para uma visão interdisciplinar. Rio de Janeiro: Editoria Central da Universidade Gama Filho, 90-171.
- Chew, D., Tollit, M. A., Poulakis, Z., Zwickl, S., Cheung, A. S., & Pang, K. C. (2020). Youths with a non-binary gender identity: a review of their sociodemographic and clinical profile. *Lancet Child Adolesc Health*, 4(4), 322-330. doi:10.1016/s2352-4642(19)30403-1
- Dickenson, J. A., Diamond, L., King, J. B., Jenson, K., & Anderson, J. S. (2020). Understanding heterosexual women's erotic flexibility: the role of attention in sexual evaluations and neural responses to sexual stimuli. *Social Cognitive and Affective Neuroscience*, 15(4), 447-465. doi:10.1093/scan/nsaa058
- Grabowska, A. (2017). Sex on the brain: Are gender-dependent structural and functional differences associated with behavior? *J Neurosci Res*, 95(1-2), 200-212. doi:10.1002/jnr.23953
- Hines, M. (2020). Neuroscience and Sex/Gender: Looking Back and Forward. J Neurosci, 40(1), 37-43. doi:10.1523/jneurosci.0750-19.2019
- Jahanshad, N., & Thompson, P. M. (2017). Multimodal neuroimaging of male and female brain structure in health and disease across the life span. *J Neurosci Res*, 95(1-2), 371-379. doi:10.1002/jnr.23919
- Joel, D. (2021). Beyond the binary: Rethinking sex and the brain. *Neurosci Biobehav Rev, 122*, 165-175. doi:10.1016/j.neubiorev.2020.11.018
- Kagerer, S., Klucken, T., Wehrum, S., Zimmermann, M., Schienle, A., Walter, B., . . . Stark, R. (2011). Neural Activation Toward Erotic Stimuli in Homosexual and Heterosexual Males. *Journal of Sexual Medicine*, 8(11), 3132-3143. doi:10.1111/j.1743-6109.2011.02449.x
- Khorashad, B. S., Khazai, B., Talaei, A., Acar, F., Hudson, A. R., Borji, N., . . . Mueller, S. C. (2020). Neuroanatomy of transgender persons in a Non-Western population and improving reliability in clinical neuroimaging. *Journal of Neuroscience Research*, 98(11), 2166-2177. doi:10.1002/jnr.24702
- Louro, G. L. (1997). Gender, Sexuality and Education. Rio de Janeiro: Voices.
- Manzouri, A., & Savic, I. (2018). Cerebral sex dimorphism and sexual orientation. *Hum Brain Mapp*, 39(3), 1175-1186. doi:10.1002/hbm.23908

- Marrocco, J., Einhorn, N. R., & McEwen, B. S. (2020). Environmental epigenetics of sex differences in the brain. *Handb Clin Neurol*, 175, 209-220. doi:10.1016/b978-0-444-64123-6.00015-1
- Moshman, D. (2014). Sexuality development in adolescence and beyond. *Human Development*, 57(5), 287-291.
- Pallayova, M., Brandeburova, A., & Tokarova, D. (2019). Update on Sexual Dimorphism in Brain Structure-Function Interrelationships: A Literature Review. Appl Psychophysiol Biofeedback, 44(4), 271-284. doi:10.1007/s10484-019-09443-1
- Raznahan, A., Lee, N. R., Greenstein, D., Wallace, G. L., Blumenthal, J. D., Clasen, L. S., & Giedd, J. N. (2016). Globally Divergent but Locally Convergent X- and Y-Chromosome Influences on Cortical Development. *Cerebral Cortex*, 26(1), 70-79. doi:10.1093/cercor/bhu174
- Rice, W. R., Friberg, U., & Gavrilets, S. (2016). Sexually antagonistic epigenetic marks that canalize sexually dimorphic development. *Mol Ecol*, 25(8), 1812-1822. doi:10.1111/mec.13490
- Roselli, C. E. (2018). Neurobiology of gender identity and sexual orientation. *J Neuroendocrinol*, 30(7), e12562. doi:10.1111/jne.12562
- Safron, A., Sylva, D., Klimaj, V., Rosenthal, A. M., & Bailey, J. M. (2020). Neural Responses to Sexual Stimuli in Heterosexual and Homosexual Men and Women: Men's Responses Are More Specific. *Archives of Sexual Behavior*, 49(2), 433-445. doi:10.1007/s10508-019-01521-z
- Schudson, Z. C., & Morgenroth, T. (2022). Non-binary gender/sex identities. *Curr Opin Psychol*, 48, 101499. doi:10.1016/j.copsyc.2022.101499
- Silva, T. (1999). Documentos de Identidade. Um aintridução às teorias do currículo. Belo Horizonte: Autêntica. doi.org/10.1590/S0104-40602009000300004
- Stoller, R. J. (2020). Sex and gender: The development of masculinity and femininity: Routledge.
- van Heesewijk, J., Steenwijk, M. D., Kreukels, B. P. C., Veltman, D. J., Bakker, J., & Burke, S. M. (2022). Alterations in the inferior fronto-occipital fasciculus - a specific neural correlate of gender incongruence? *Psychol Med*, 1-10. doi:10.1017/s0033291721005547