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Factors that may influence brain gender development

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ABSTRACT

Brain development begins in the prenatal period and continues through the early postnatal years, reaching near-adult size and organization by approximately 3-4 years of age. Brain gender differentiation is initiated during prenatal and early postnatal stages, while the sexual behaviors typically emerging later after puberty. Most the majority of research on brain gender dimorphism and sexual orientation has focused on prenatal mechanisms, whereas the contribution of early postnatal development remains less well characterized. This review synthesizes current evidence on brain gender differentiation across prenatal and early postnatal periods, with particular emphasis on central nervous system dimorphism and factors influencing sex-related developmental trajectories. A review specifically examines the potential role of environmental and circumstantial influences, including chemical exposures, stress, and other internal and external factors, during the neonatal and early postnatal stages. We propose that these underexplored periods may play a significant role in shaping later gender-related and behavioral outcomes. More studies will be essential to better understanding of environmental influences on brain gender development and sexual orientation.

Introduction

Sex differences in brain development and their relationship to gender identity and sexual orientation remain a central question in neuroscience, psychology, and behavioral biology. While sex is typically defined by biological characteristics such as chromosomes, hormonal profiles, and reproductive anatomy, gender identity reflects an individual's internal sense of self, and does not necessarily conform to a strict binary classification. Accumulating evidence suggests that brain development related to gender exists along a spectrum with overlapping but partially dimorphic features in structure and function.

The structure of the brain's functional centers and the perception of information may vary from person to person, however certain differences have been found between the female and male brains. For example, studies indicate that males tend to outperform females in behavioral tasks tapping visuospatial and navigational skills, whereas females tend to score higher on tasks assaying verbal and social skills [1]. Additionally, females often demonstrate superior performance in object location memory [2-3], emotion recognition [4-5] and empathy [6], while males are more likely to exhibit higher levels of aggression and behavioral disinhibition [1, 7]. These findings support the concept of sexual dimorphism in certain brain structures and functions, although considerable overlap exists between individuals.

A substantial body of research indicates that both gender identity and sexual orientation are shaped by biological processes during early development, including the effects of gonadal steroid hormones, gene expression, and maternal factors [8]. Yet, most research on brain gender dimorphism and sexual orientation has focused predominantly on the prenatal development, leaving the postnatal period comparatively underexplored. This early life stage marked by rapid brain growth and development, and in males, a transient surge in gonadal androgens, suggesting that it may represent a critical window for further brain gender differentiation.

Emerging evidence suggests that this early postnatal window may represent a sensitive developmental period during which environmental and physiological factors can influence neural organization. External factors during this newborn/infant period may disrupt normal gender differentiation processes and influence sexual orientation in adulthood. The influence of such postnatal factors on subsequent gender-related behavior and sexual orientation remains poorly understood.

This review provides an integrative synthesis of current knowledge on brain gender differentiation and examines the potential role of postnatal developmental processes in shaping gender identity and sexual orientation. It highlights the hypothesis that environmental factors during the neonatal and early postnatal period may contribute to long-term behavioral outcomes, emphasizing an important postnatal window limited attention in the existing literature.

Prenatal brain development

The brain commences development during the third week of embryonic development. At this stage, neuroprogenitor cells proliferate, migrate and differentiate into neural cells. In the fourth week of development, fusion of the neural tube folds in the cranial region and closure of the rostral neuropore culminate in the formation of three brain regions: the forebrain, midbrain and hindbrain (rhombencephalon). During the fifth week of development, the forebrain subdivides into the telencephalon and diencephalon, while the midbrain remains undivided and the rhombencephalon differentiates into the metencephalon and myelencephalon, thereby establishing five brain regions [9]. Pronounced prenatal brain development occurs in month nine of gestation, when the brain undergoes a threefold increase in volume.

Human male and female embryos develop similarly in the first six weeks of gestation, regardless of genetic sex. At approximately weeks 6-7 of development, sexually dimorphic gonads develop under the influence of the X chromosome in females or the Y chromosome in males [10]. Expression of Y-linked genes stimulates the differentiation of testicular Leydig cells, which begin to secrete testosterone in week 8 [11]. Androgen production increases concomitantly with Leydig cell proliferation and hypertrophy driven by human chorionic gonadotropin, and testosterone reaches peak levels at 15-18 weeks of gestation [12].

Prenatal brain gender development

Fetal gonadotropins sustain testosterone production and promote masculine differentiation. Testosterone and its derivative, dihydrotestosterone (DHT), induce the differentiation of the male reproductive system. Gender differentiation of the genitals occurs during the first trimester of pregnancy, whereas brain gender differentiation takes place in the second trimester, coinciding with the presence of embryonic testosterone secretion in males and its absence in females, which persists into the third trimester [13].

According to the classical theory, prenatal exposure to testosterone drives male-typical development (masculinization), whereas female-typical development (feminization) occurs in its relative absence. Female monkeys exposed to androgens early in development exhibit masculinization of sexual behavior [14-15], rough play, grooming [14] and some learning abilities [16]. The periods during which testosterone induces brain gender differentiation correspond to the times when testosterone levels are highest in males compared to females [17]. In humans, the testicular elevation in testosterone levels occurs between months 2 (about 7-8 weeks of gestation) and 6 of pregnancy [11], which coincides with surges in pituitary gonadotropin secretion [17-18]. Testosterone levels then decline gradually until birth.

The study of sexual orientation dates back to the early 1930s, when estradiol was shown to induce lordosis (the sexually receptive posture of a female mammal to facilitate mating) in castrated male rats and that estradiol-treated intact rats display lordosis as well as mounting and ejaculation [19-20]. A landmark discovery in 1959 demonstrated that prenatal testosterone treatment organized the female guinea pig brain into a male-typical pattern and resulted in a permanent reduction in behavioral sensitivity to estrogen [21]. In the late 1950s, it was shown that testosterone administered to pregnant guinea pigs resulted in hermaphroditic female offspring with ovaries and masculinized genitalia [21]. In adulthood, these females exhibited more male-typical behaviors and fewer female-typical behaviors compared to control. These findings led to the hypothesis that androgens act as morphogenic agents during the prenatal period, permanently shaping the neural circuits that mediate mating behavior. Supporting this, two female rhesus monkeys treated prenatally with testosterone exhibited masculinization of sexually dimorphic social behaviors and developed pseudohermaphroditic characteristics [22]. Mounting of peers and rough play by females positively correlated with the duration (15-, 25-, and 35-day testosterone treatments) of exposure during gestation [23]. Numerous sexually dimorphic behaviors observed in human children, resemble those programmed by androgens in young rhesus monkeys, including rough and tumble play [24-25], playmate choice [26] and interest in young infants [27-28]. Some of these behaviors have been reported to shift towards male-typical patterns in human females exposed prenatally to high levels of androgens [26, 29-31].

Although the precise mechanisms underlying neural organization of primate and rodent behaviors remain unclear, androgens likely influence fundamental developmental processes, including neuron migration, cell differentiation, apoptosis, and/or synaptic proliferation. During gestation, the basic neural circuits that underlie

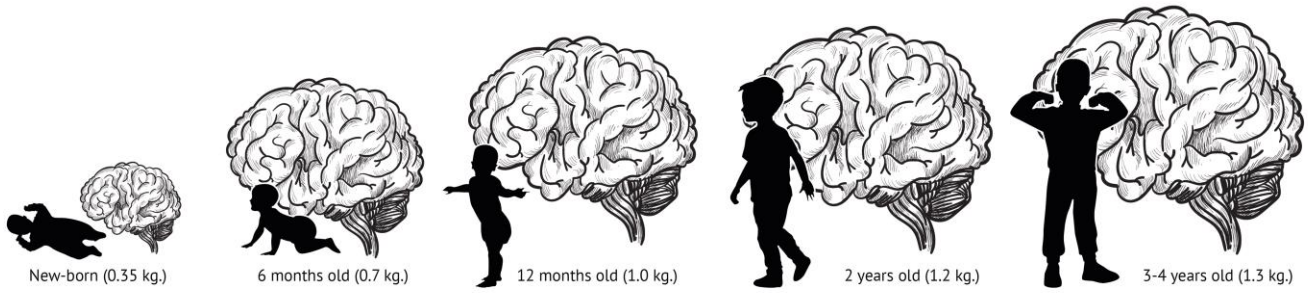
juvenile and adult behaviors are established through a complex, time-dependent process, with sensitive periods reflecting the developmental timelines of the circuits [32]. The presence or absence of androgens during these sensitive periods may direct their development toward a male-typical or female-typical trajectory independently of the others. In parallel, prenatal androgen exposure may act upon neural areas, including motivational or reinforcing circuits, responsible for more general brain functions and thereby influence a broad range of behaviors. These neural modifications may subsequently influence both the specific behaviors expressed and the contexts in which they occur.

Effects of prenatal stress, applied from day 14 of gestation, on sexual behavior were evident when comparing plasma corticosterone levels between control and treated rats [33-34]. Male offspring of females stressed during pregnancy showed markedly reduced plasma testosterone levels during gestation and at birth, accompanied by reduced copulatory behavior in adulthood, which was rescued in some males following daily administration of 1 mg of testosterone propionate for 6 weeks [35-38]. Males whose mothers experienced environmental stressors during pregnancy, exhibited abnormally elevated levels of female lordotic behavior in adulthood [39]. In humans, maternal stress has been associated with an increased incidence of homosexuality in both boys and girls [40-41]. Some scientists propose that prenatal androgens constitute the primary biological determinant of male gender identity, even in the absence of the neonatal and pubertal androgen surges [42]. Limited data exist regarding the timing of androgen effects during the neonatal/postnatal period.

Neonatal brain and gender differentiation

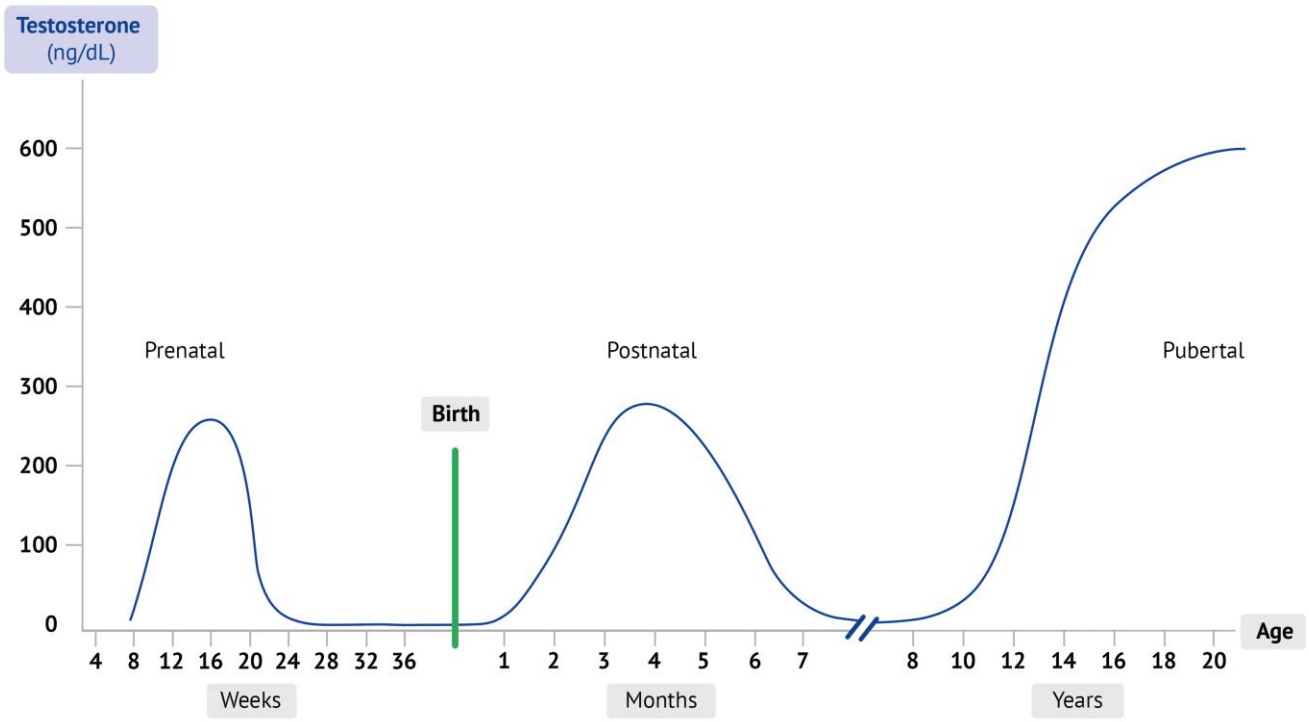
At birth, the human brain contains approximately 100 billion neurons and weighs 0.35 kg, representing roughly 25% of the weight of an adult brain. During the first six months, its weight doubles; it reaches approximately 1 kg at 1 year and approximately 1.2 kg at two years and, by five to six years, it attains the adult weight of around 1.3 kg [43-44]. Although the most rapid phase of brain growth occurs within the first six months of birth, structural and functional brain development continues throughout the first three to four years (Figure 1). Throughout this period, new neurons, synapses and neuroglial cells are formed, and multiple brain nuclei, functional centers and neural interconnections mature. The early postnatal period has therefore been suggested a critical window for the development of sexually dimorphic cognitive function, including spatial ability [45]. The factors contributing to brain gender differentiation remain a subject of considerable debate in the literature. Accumulating evidence indicates that sex hormones influence the sexual differentiation of the brain or specific brain regions, producing long-lasting effects on human behavior, while heritability studies highlight the contribution of genetic factors [46].

Figure 1. Postnatal brain growth.



Testicular testosterone levels rise again during the first 3 months of the postnatal period [11], coinciding with surges in pituitary gland gonadotropins [18], and subsequently decline until the end of the sixth month. The first 1-5 postnatal months, corresponding to peak testosterone levels in male infants, are therefore considered a sensitive period for sexual differentiation of the brain [13] (Figure 2). The pituitary-testicular axis of the neonate responds to exogenous gonadotrophin-releasing hormone (GnRH) similarly to adults [47-48], suggesting that the central nervous system (CNS) mechanism regulating this axis is already functionally mature at birth. The period may be a critical interval in the development of binding sites (receptors) on GnRH neurons [49]. Observations in individuals, who were sex-reassigned to females at birth and later (usually during puberty) declared themselves male, suggest that the first prenatal testosterone surge is most important for the development of gender identity [42]. Yet, the second testosterone surge during the neonatal or early postnatal period may also contribute to gender identity formation. Studies in primates indicate that the period corresponding to the neonatal testosterone peak is the critical window for the sexual behavioral development [49]. However, others argue that sexual behavior is not influenced by testosterone expressed in the postnatal period. At present, evidence supporting postnatal influences on human brain gender development and sexual orientation remains indirect, and hypotheses regarding the role of the neonatal testosterone surge should be interpreted as provisional pending targeted human studies. Specifically, blocking the early postnatal testosterone rise with a GnRH antagonist did not alter sexually dimorphic behaviors, such as rough and tumble play or mounting in monkeys [48, 50]. Similarly, neonatal castration had no impact on these behaviors [51-53]. After the postnatal period, testosterone levels decline to a minimum until onset of puberty. From puberty onwards, sex hormones activate the function of previously organized neuronal systems ("activating effects") [18]. The timing of pubertal onset has been linked to sexual orientation in men [54], with homosexual men experiencing puberty earlier than heterosexual men, whereas no such association has been observed in woman [55]. Estrogens may also have an effect on sexual behavior. Nonhuman primate females show increases in sexual behavior and sexual initiation behaviors around the time of ovulation [56-57]. Gonadectomy in females reduces receptive behavior, whereas estradiol replacement restores it [58-59]. Estradiol also enhances sexual initiation in gonadectomized females, independently of male sexual interest and behavior [59].

Figure 2. Testosterone secretion at prenatal, postnatal and pubertal periods.



For many years, feminization was considered a passive process, occurring in the absence of high androgen levels. However, accumulating evidence demonstrates that estradiol plays an active organizational role in the brain, one of the best-characterized examples being the cyclic formation and breakdown of excitatory synapses in the hippocampus [60-61]. Despite these insights, the organizational effects of ovarian estrogens on human behavior during early development remain poorly understood.

Brain neural centers associated with sexual dimorphism

Generally, the left and right hemispheres of the brain exhibit structural and functional differences. Neuroimaging studies provide substantial evidence for sexual dimorphism in the human brain, manifesting as subtle but consistent differences in brain anatomy and functional organization between males and females [62-63]. Male brains show more hemispheric asymmetry and regional differences in grey matter volume, whereas female brains display greater hemispheric symmetry [64]. Moreover, women and men differ in the neural circuits they employ for information processing, including listening, reading, language and emotion. For example, women typically engage both hemispheres when processing language, whereas men utilize the left hemisphere only [65]. Men are more likely to recruit localized regions on just one side of the brain, for a specific task, while women typically tend to engage more distributed bilateral networks for the same task [66]. These sex-related differences in neural organization have been partly attributed to the organizing effects of sex hormones on the CNS [67].

The corpus callosum, the principal commissural region of the brain connecting the left and right cerebral hemispheres, exhibits pronounced sexual dimorphism. On average, the cross-sectional area of the midsagittal corpus callosum is larger in females than in males. Sexual dimorphism has also been observed in the caudal region of the human corpus callosum, a structure that may contribute to reported sex differences in spatial abilities [68]. Furthermore, men tend to exhibit greater intra-hemispheric connectivity, whereas women demonstrate greater interhemispheric connectivity via the corpus callosum [65].

The sexually dimorphic nuclei (SDN), also referred to as the interstitial nuclei of the anterior hypothalamus (INAH), is a cluster of neurons within the medial preoptic area (POA), that differs in both size and cell number between males (0.2 mm^3) and females (0.1 mm^3), particularly in rodents and humans. These differences suggest a role for the SDN in sexual behavior, other sex-related functions and brain differentiation [69]. The SDN of the medial preoptic area is organized prenatally under the influence of testosterone [70], but a role for postnatal androgen in its development has also been demonstrated [71]. The SDN is identifiable by four years of age, suggesting that perinatal testosterone secretion contributes to its development [69]. In girls, the SDN undergoes a reduction in cell number during prepubertal development, contributing to sexual dimorphism [69]. It has been proposed that testosterone secretion in males promotes cell survival within the SDN by counteracting the programmed cell death that occurs in females [72].

Four interstitial nuclei of the anterior hypothalamus (INAH1–INAH4) have been identified; among these, the third (INAH3) has been reported to be smaller in homosexual men as compared with heterosexual men and comparable in size to that of women [73]. In animal studies, ablation of the SDN resulted in males exhibiting either neutral or androphilic preferences [74]. Collectively, these findings support the hypothesis that the sexually dimorphic brain provides an anatomical substrate for psychosexual development, shaped by gonadal hormone exposure during prenatal, postnatal and pubertal periods.

Additional sexually dimorphic brain regions are the bed nucleus of the stria terminalis (BNST) and the amygdala, both components of the limbic system, which regulates fear, anxiety, social behavior and motivation. These structures play a central role in mediating behavioral and autonomic responses to stressors. The amygdala is considered the core component of a neural circuitry responsible for detecting and processing fearful and threatening stimuli and for initiating appropriate fear-related and defensive behaviors. It also contributes to decision-making and emotional responses, such as fear, anxiety and aggression. The amygdala and BNST are anatomically and functionally interconnected, and are often referred to as the "extended amygdala". The volume of the BNST is larger in men than in women, reflecting sexual dimorphism in both structure and function [75]. Notably, the size of this brain region in male-to-female transgender individuals was reported to be comparable to that observed in cisgendered women (i.e., individuals whose gender identity aligns with their sex assigned at birth) [76]. Additionally, sex differences have been identified in receptor distribution within the amygdala; in men, the right amygdala exhibits a high density of androgen receptors, whereas in women, the left amygdala shows a higher density of estrogen receptors [77].

The mammillary bodies and the hippocampus are anatomically interconnected structures essential for memory processes, particularly spatial navigation and recollective memory, as demonstrated in both clinical populations and animal models [78]. This circuit is also implicated in the regulation of various aspects of sexual behavior, including penile erection [79]. The most pronounced sex differences in androgen receptor distribution are observed in the lateral and medial mammillary nucleus. Sex differences in androgen receptor distribution have also been documented across multiple hypothalamic regions, including the horizontal diagonal band of Broca, the sexually dimorphic nucleus of the medial preoptic area, the dorsal and ventral zone of the periventricular nucleus, the paraventricular nucleus, the supraoptic nucleus, the ventromedial hypothalamic nucleus and the infundibular nucleus [80].

The hypothalamus and pituitary gland play a central role in the hypothalamic-pituitary-gonadal (HPG) axis providing a communication pathway that enables neuroendocrine signaling between

the brain and the gonads. Recent transcriptomic studies have demonstrated sex-specific differences in gene expression within the hypothalamus and pituitary gland. In a mouse model, three hypothalamic transcripts and 43 pituitary transcripts were found to be differentially expressed between sexes [81]. Gonadotropes isolated from juvenile males and females, from cycling females at different stages of the cycle, and from adult males, exhibited unique gene expression profiles, with approximately 100-500 genes expressed uniquely at each developmental stage or cycle phase. The differentially expressed genes were significantly enriched in the GnRH, calcium signaling and MAPK signaling pathways, highlighting molecular plasticity within the gonadotrope population [82].

Glial cells as a target for sex hormones

Cell-level organization in the brain exhibits sex-dependent differences. Astrocytes are a key glial cell type involved in synaptic plasticity and play a role in learning and memory as well as in maintaining brain homeostasis. They form interactions with other brain cells, such as neurons, glial cells and vascular elements through their extensive processes, and play a crucial role in regulating brain activity, ranging from synaptic transmission to the formation, maintenance and regulation of the blood-brain barrier (BBB). At least ten distinct astrocyte morphologies have been identified, reflecting their structural and functional heterogeneity within the central nervous system. While the overall number of astrocytes in the brain does not differ between males and females, regional sexual dimorphism in both their density and morphology is evident. In addition, significantly differential expression has been measured for 105 genes in astrocytes from human males versus females [83]. For example, zinc finger transcription factor (ZFX) expression is significantly elevated in female compared to male astrocytes. This transcription factor has been shown to contribute to the accumulation of hyperphosphorylated tau, leading to the formation of neurofibrillary tangles, a pathological hallmark of Alzheimer's disease. Notably, Alzheimer's disease exhibits a pronounced sex bias, affecting women at approximately twice the rate observed in men [83-84]. The glutamate receptor mGluR3, which is abundantly expressed in hippocampal and cortical astrocytes, has been found at reduced levels in females compared to males, and has been associated with memory loss in women [85]. Both male and female human astrocytes express estrogen receptors (ER) [86], including ERα, ERβ and G protein-coupled estrogen receptor 1 (GPER). However, female astrocytes appear to be more responsive to estrogen than male astrocytes, likely due to higher expression of ERs. In contrast, male astrocytes were reported to exhibit lower surface ER density and to reach full maturation more rapidly than female astrocytes [87]. Hypothalamic astrocytes from male rats are unable to produce progesterone in response to estrogen due to lower receptor expression [88] and absence of elevated luteinizing hormone (LH) levels [89]. Sex differences have been reported to specifically influence astrocyte development and activity, as evidenced by differential expression of glial fibrillary acidic protein (GFAP), and may contribute to varying susceptibility to neurodegenerative diseases. In animal models, estrogen has been shown to modify astrocyte morphology in ways that could affect their interactions with neurons and other cells in the brain [90]. Astrocytes and other glial cells may represent an additional layer of sex-specific neural regulation, however, direct evidence linking glial mechanisms to behavioral outcomes relevant to brain gender development or sexual orientation is currently limited.

Pathologic conditions affect gender differentiation and sexual orientation

Direct androgen effects on the brain can be observed in pathologic genetic conditions, such as complete androgen insensitivity syndrome (CAIS),

which arises from mutations in the androgen receptor gene located on the X chromosome (Xq11-12), resulting in androgen receptor dysfunction. CAIS occurs in individuals with a XY karyotype who are unable to respond to androgens. The SRY gene, present on the Y chromosome, normally initiates a cascade of events responsible for male sexual differentiation, including testes formation. Although individuals with CAIS have normal testicular function and produce physiological levels of testosterone, the absence of functional androgen receptors prevents tissue responsiveness, leading to female-typical phenotype, with differentiation of the external genitalia and other features characteristic of feminized sexual development. Such individuals are typically raised as females and often remain undiagnosed until adolescence, when they present with primary amenorrhea. They typically report sexual attraction, fantasies and experiences consistent with female and heterosexual orientations [91], suggesting that direct androgen action on the brain plays a crucial role in the development of male gender identity and male heterosexual orientation, which are highly dependent on androgen exposure during the fetal period [91-92]. Evidence from studies of women with congenital adrenal hyperplasia (CAH), a condition characterized by excessive androgen exposure, supports this notion. These women often present with masculinized external genitals, and exhibit more cross-gender-typical role behavior and patterns during childhood [93], including a preference for typically male toys [94] and playmates [94-95]. Compared to control females, CAH females have been reported to be more aggressive [96], less interested in infants [28] and to describe themselves as less empathic and maternal [97]. Furthermore, CAH females are more likely to report sexual attraction to women than their unaffected sisters [26]. Taken together, findings from CAH and CAIS populations suggest that androgens play a central role in the development of sex-typed behavior and gender identity.

External factors affect sexual orientation

Several works have reported that external factors, such as chemical exposure, psychosocial stress and environmental influences, may alter aspects of brain gender differentiation, and consequently, sexual orientation. For example, gestational exposure of female mice to tributyltin chloride (TBT) was shown to modulate the neuropeptide Y system within the paraventricular nucleus, resulting in reduced immunoreactivity in both sexes and in a profound, long-term, sex-specific effect [98]. Prenatal exposure to certain substances, such as nicotine, has been associated with an increased likelihood of lesbianism. Similarly, maternal stress during pregnancy has been linked to an increased likelihood of homosexuality in male offspring. Although prenatal maternal stress has been hypothesized to influence sexual orientation through neuroendocrine pathways (elevated cortisol may suppress fetal testosterone and influence male-typical brain differentiation), evidence in humans remains limited and inconsistent. By contrast, postnatal social and familial environmental factors, such as being raised by transgender or homosexual parents, do not influence a child's sexual orientation [99-100]. Prenatal endocrine-disrupting chemicals (EDCs) exposures are associated with sex-specific deviations in biological aging, which may have lasting implications for child health and development [101]. DNA methylation at autosomal CpG sites of genes had lower levels in male than in female newborns [102]. Exposure to elevated scrotal temperature during the neonatal period, resulting, for instance, from prolonged diaper use, may affect testicular cells to produce normal testosterone level [103], which could theoretically influence brain gender differentiation and subsequent sexual orientation. Research from epigenetic [101-102] and longitudinal cohort [104] studies demonstrates that prenatal and early-life biological signatures, including DNA methylation patterns, can be tracked across development and relate to sex-specific outcomes.

Recently it was shown that even single-nucleotide mutation in DNA enhancer, essential for sex gene expression, produce the complete XX female-to-male sex reversal [105]. Epigenetic associations with prenatal chemical exposures in infancy further illustrate how environmental factors may leave durable molecular signatures. At least one large prospective birth cohort has examined multiple prenatal and postnatal predictors of adolescent sexual orientation, integrating early life biological markers with long-term outcomes. These longitudinal designs complement classical endocrinology by linking early exposure windows, molecular regulation, and later behavioral traits.

Summary

Although this review touches on multiple aspects of brain development, these are discussed within a single conceptual framework: the role of early postnatal processes in brain gender differentiation. Evidence suggests that development of male gender identity and male heterosexual orientation critically depends on direct androgen action on the brain during its early developmental stages. In contrast, female gender identity is thought to develop in the relative absence of male sex hormones, however, the results of recent years show the involvement of estrogens as well. Most existing data on brain gender differentiation and sexual orientation, both of which become apparent after puberty, are derived from studies focusing on the prenatal period, whereas limited information exists regarding the early postnatal period, a critical phase of rapid brain growth and development that coincides with testosterone peaks in males, but not in females. It has been proposed that both the neonatal and early postnatal periods play a pivotal role in shaping gender-specific brain organization and sexual orientation. Furthermore, exposure to exogenous factors such as phytoestrogens, stress, diapers, plastics and chemicals, hypothetically may influence brain gender development and sexual orientation during the neonatal and postnatal stages. Animal models offer critical mechanistic insight into the hormonal organization of the brain, however, species-specific differences necessitate caution when extrapolating these findings to complex human traits such as gender identity and sexual orientation. Many early studies in this field were conducted within conceptual and methodological frameworks that differ substantially from current understandings of gender and sexual orientation, which may limit the interpretability and applicability of some findings.

Conclusions

Further scientific, contemporary, interdisciplinary, and methodologically rigorous studies are needed to better elucidate the influence of various factors during the postnatal period on human brain gender-specific development and sexual orientation. Future progress in this area will likely depend on prospective cohort studies that capture hormonal, clinical, and environmental data during the early postnatal period and follow individuals longitudinally into adolescence and adulthood.

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