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Neurobiology of Gender and Behavior

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Introduction to Neurobiology

Neurobiology is the scientific study of the nervous system. In recent years, this field has experienced tremendous growth. It can now be viewed as a cohesive area of study, which provides a multidisciplinary platform for the development of a literature on gender. While many issues remain to be explored, neurobiological research has already revealed essential aspects for understanding gender and the biological bases of behavior. An established scientific understanding of the link between biology and behavior will assist research in this field, as well as help the general public develop a positive perspective on gender.

Historical Perspectives on Gender and Behavior

The question of why males and females exhibit fundamentally different behaviors has drawn interest since antiquity. Early speculation by Hippocrates suggested brain differences as the basis for sex-linked behavioral patterns. Subsequent investigations covered genetic, neurobiological, hormonal, and environmental influences, among others.

Modern inquiry began from the study of sex differences in animals. Early work revealed a genetic basis for these differences, with males of various species tending to be more aggressive than females. Understanding of underlying genetic influence expanded with the identification of the SRY gene, which regulates the development of male-specific underpinnings. Genetic differences alone, however, are insufficient to explain the observed behavioral patterns, which require the function of neural circuits within a complex neurobiological framework. Sex differences have also been examined across the dimensions of brain anatomy, functional connectivity, and plasticity of the central nervous system [1].

Characterization of sexual dimorphism within mammalian brain structures represented a major milestone in understanding of the neurobiological investigation of sex differences. One widely studied structure, the sexually dimorphic nucleus of the preoptic area, gives rise to sex-specific behaviors in androgen-exposed rodents. Components of sexual dimorphism extend to regional volumes, axonal and dendritic morphology, synaptic pattern, and electrophysiological properties, among others. Sexual dimorphism influences a broad range of phenotypic traits, from cognition to disease susceptibility.

The Role of Genetics in Gender Differences

Human gender responses are neither wholly biologically set nor entirely constructed by culture and experience. Recognition of significant biological underpinnings to aspects of gender received public attention through scientific committee assessments of programming influences. Norms reflecting and reinforcing information about the personalities of individual dogs are massively larger than those based on gender. More precise estimates require study of "core gender identity"—a strong and persistent preference to be regarded as a member of the opposite or an alternative gender—and stereotyping. Data from individuals, including intersex persons, transcultural studies, various natural experiments, and comparisons with nonhuman animals provide converging evidence linking social attitudes to neurobiology [1]. Even when neuroanatomical effects are small, their correlation with distinct developmental programs or their influence on how individuals respond to experience and hormones suggests wide-ranging consequences.

Genetic, epigenetic, and hormonal mechanisms collaborate to establish sexual differentiation. The whole-body phenotype develops along one of two discrete developmental pathways following the decision driven by the sex chromosome complement [2]. The early formation of the primary sensory apparatus in a fetus appears to shape the primary and socializing gender orientations of humans.

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Hormonal Influences on Behavior

Behavior is modulated by circulating sex hormones in adulthood, which are linked to dimorphic brain structure and function [1]. As steroid hormone receptor expression can be found in both within neural regions that exhibit dimorphism and in regions that are itself dimorphic, circulating sex hormones likely regulate the structure and function of multiple brain regions. During gestation, gonadal steroid hormone secretion organizes many sexually dimorphic aspects of the brain; gonadal sex thus strongly influences postnatal morphology. Steroid hormone secretion continues to shape the adult brain. Rodent sexual behavior changes dramatically across the estrous cycle, for example, suggesting continuing hormone regulation of circuits that control behavioral output. Non-reproductive behaviors, such as certain foraging routines, also show hormone-dependent sexual differentiation in adulthood. Circulating hormones can modulate the expression of neural dimorphism, both by regulating postnatal neural structure and by controlling the neural response to the stimulus environment. Differential exposure to circulating gonadal hormones represents an obvious causal factor in global shifts in dimorphism during the postnatal period. Continuing sex differences in steroid hormone secretion outside of the perinatal window have been documented across a wide range of species. Systems-level behavioral change seems to be associated with circulating gonadal hormones during adolescence and adulthood.

Neuroanatomy of Gender Differences

The presence of structural sex differences in animal brains has been recognized for over a century, offering insight into the neurobiology of gender. Historically, literature has examined how anatomical sexual dimorphisms relate to behavior, advancing from isolated neuroanatomical studies to integrated functional behavioral research. Contemporary experimental and theoretical contributions seek to elucidate how neuroanatomical, genetic, and hormonal variations between sexes translate into distinct behavioral patterns. Sexual dimorphism in the brain is evident across multiple levels, and these anatomical differences influence connectivity across numerous functional circuits [1]. Circumscribing the central nervous system into well-defined category-specific regions remains challenging, as the concept of brain specialization is nuanced. However, it is clear that while many brain areas participate in functions common to both genders (e.g., appetite regulation, locomotion, cognition, emotional processing), substantial variations are observed. Furthermore, several regions—many associated with social behavior—exhibit a high density of anatomical sex differences. Early modifications in these systems may produce enduring functional consequences.

Investigations into sex differences often encompass two principal domains: susceptibility to neurological or psychiatric disorders and cognitive capabilities such as language and spatial skills. Such differences are widely documented both in humans and animal models [3]. In humans, the enhanced spatial abilities observed in males have been linked to hormonal exposure during prenatal and postnatal development, suggesting a biological underpinning that emerges early in life. Emotionally charged stimuli tend to provoke higher activity levels in specific brain regions of women compared to men, with women being more responsive to social cues—a phenomenon associated with higher incidences of affective disorders.

Sexual Dimorphism in Brain Structure

Human brains exhibit many sex-related differences, ranging from patterns of gene expression to subtle anatomical variations. Male-female differences in brain structure, functional connectivity, chemistry, and electrical activity have been reported for most major brain regions [1]. Inevitably, discussion of the neurobiology of gender focuses largely on sexual dimorphism—the systematic difference in form between genitalia in males and females, as well as many secondary sex characteristics. Such differences also exist within the brain; the bed nucleus of the stria terminalis, the central medial amygdala, the interstitial nucleus of the anterior hypothalamus, and several other neural populations are substantially larger in males than females.

Functional Connectivity Variations

Intrinsic functional networks (RSNs) of the brain are assemblies of interrelated circuitry, underlying sensors, motor functions, affective states, and cognitive integration. These functionally linked brain areas are identifiable in resting-state functional magnetic resonance imaging (rs-fMRI) data. rs-fMRI allows nondirected, task-free measurement of blood oxygenation level-dependent (BOLD) signals that indirectly index neural activity when participants lie still and awake in the scanner. Analyzing variation of whole-brain BOLD signal can reveal spatially distributed systems that rise and fall synchronously over time, and statistical decomposition can resolve the signal into separable systems. Many different analytic approaches point to the existence of temporally synchronous systems (networks) across the brain at detected frequency peaks. These networks resemble architecture otherwise observed in response to directed task demands [4]. Sex-related differences in intrinsic functional brain organization are widely reported for the adult brain. Connectivity analyses of RSNs support the idea that males and females establish different patterns of brain network architecture. Modeling sex as a biological variable in rs-fMRI analysis is therefore required; higher-order models may be more sensitive to sex-related differences.

Sex-related differences in large-scale brain networks are more strategically prominent in the central executive (CEN) and default mode (DMN) portions. Dimorphisms extend to the cerebellar RSN, where males exhibit stronger cerebellum-to-DMN connectivity and spatially broader neuronal coherence of cerebellar RSNs. This is consistent with the cerebellum's involvement in frontoparietal control, linking cerebellar dysfunction with dysfunction in multiple higher-order association systems that underpin complex behaviors and cognition.

Published analyses of large populations of gynephilic cisgender and transgender persons reveal that receptors implicated in sexual differentiation of the brain have specific allele combinations, implicating estrogen and androgen receptors in brain development. Differences in gender variants are not restricted to a single network but involve multiple networks, particularly the frontoparietal network implicated by own's-body-perception hypotheses. A complex brain function controlling congruency between assigned sex and feeling of gender requires interactions between large-scale networks, supporting use of a whole-brain functional connectivity approach to investigate network differences. Data confirm predictions from both the cortical-neurodevelopmental and the own's-body-perception hypotheses, suggesting some modifications to the latter. Notably, lesser fronto-parietal connectivity strength in trans men fits own's-body-perception predictions. Brain-network interactions indicate these hypotheses are complementary [5].

Cognitive Differences Associated with Gender

Males have larger total brain volumes and more single-hemisphere brain sites showing strong functional connections. Symmetry favors right-hemisphere lateralization in males and left-hemisphere dominance in females. A largely bilaterally connected pattern centered on the posterior cingulate is consistent across sexes. Women tend to excel in reading, verbal fluency, recognition memory, and episodic memory [4].

Descriptions of gender differences in cognitive skills include visuospatial processing, perceptual speed, language and verbal skills, phonetic coding, memory, and higher-order executive function. Others involve the quantities of neurotransmitters, synaptic factors, circulating hormones, and relationships among these factors that predict particular forms of learning and information processing. Age is another important consideration. Over the course of childhood and adolescence, boys demonstrate a shift toward faster and more efficient spatial cognition that exceeds the rate observed in girls. This pattern begins to change in early adulthood and is reversed in geriatric populations, for which women show an advantage in spatial cognition. Relatedly, girls tend to excel in verbal fluency, a robust index of efficient frontotemporal function that is markedly enhanced by circulating estradiol [1]. The two findings may be mechanistically related because better frontotemporal function can compensate for poorer frontoparietal function, and vice versa.

The emergence of directionally specific sexual dimorphism in the functional organization of the human brain complements the findings of structural dimorphism generated over the past several decades through histology and neuroimaging. Because expression of sexually dimorphic behavior requires a neural correlate, the existence of patterns of directionally specific intrinsic functioning that embed discrete sex-related units of cortical and subcortical brain regions constitutes a critical advance in the continuing effort to identify corresponding dimorphisms across levels of analysis. Nevertheless, the neuroscience behind behavioral dimorphism is at best indirect, and sex differences in the brain should not be viewed as landmarks or indicators of dimorphic behaviors but as having greater implicative power for the understanding of physiological predisposition and state-dependent capability.

Spatial Abilities

Spatial skills are a collection of cognitive capabilities required to perceive, analyse, transform, and generate visual images and to understand the spatial relations of objects; these skills support a wide range of human activities such as problem-solving, mental rotation, wayfinding, map reading, and navigation. According to the current state of behavioural and neuroimaging research, individuals show large sex differences in large-scale spatial abilities and medium differences in small-scale spatial abilities. Males outperform females in both large- and small-scale spatial abilities, but the gender gap is much smaller in the latter. Both sexes employ common brain regions in these tasks; however, females exhibit distinct patterns of brain activity that also differ between large- and small-scale spatial tasks. In large-scale spatial ability, females' performance is affected by spatial anxiety and less efficient functioning of the parahippocampal gyrus. In small-scale spatial ability, females rely more heavily on egocentric strategies and exhibit less efficient sub-gyral functioning. These behavioural gender differences are largely attributable to underlying neural differences, although the causal origins of the neural disparities remain inconclusive. Evolutionary hypotheses propose that these differences evolved in response to sex-specific dispersal patterns, mating strategies, or divisions of foraging labour [6].

Verbal Skills

Vocal verbal communication skills are one of the several well-documented differences between men and women. Sex hormones during gestation affect brain regions that control the development of neural circuits in specific verbal communication domains. Up to the first three years of life, girls' neurobiological maturation in areas related to communication and language is faster and more advanced than boys'. Disorders in language and speech production show a higher prevalence in boys than in girls [7].

From an evolutionary perspective, the distinction between words and gestures was crucial for human development and brain specialization along the verbal-nonverbal gap. Language acquisition during childhood is accompanied by a sexual dimorphism in hemispheric lateralization: children using symbolic/generative language processes preferentially engage the left hemisphere, whereas children expressing themselves through non-communicative sounds and gestures engage the right hemisphere. In children, language input and early vocabulary growth relate to socioeconomic environment as well as biological factors such as fetal testosterone exposure. Earlier and more substantial experience with verbal material and communication likely facilitates the maturation of neural systems underlying verbal skills in girls [8].

Emotional Processing and Gender

Polar prostaglandins and their derivate 15-keto-metabolites, measured by liquid chromatography-mass spectrometry in pituitary membranes of mature female rats, increased distinctly after stimulation with luteinizing-hormone-releasing hormone (LHRH). This response was demonstrably larger than that found in the pituitaries of male rats.

When considering social behavior, emotional processing presents another key area of gender differentiation. Several neurobiological mechanisms shape emotional responses in sex-specific ways, and societal display norms further compound these effects. Females generally exhibit heightened responsiveness to emotionally arousing stimuli [9]. Event-related potential (ERP) studies report that women demonstrate greater neurological sensitivity to positive and neutral stimuli and stronger somatic reactions to negative stimuli, compared to men. Analysis of spectral responses to emotional stimuli reveals enhanced activity in the beta and gamma frequency ranges for females relative to males [9]. These physiological and neurobiological characteristics—often accompanied by social expectations that permit females a wider range of emotional display—contribute to well-documented, gendered differences in emotional expression that also influence social behavior. Empirical evidence for greater female responsivity to emotional stimuli, along with stronger oscillatory responses, suggests more intense cerebral processing of emotional information, which correlates with augmented behavioural expression. Such findings underscore the interconnectedness of sexual dimorphism and behavioural biosocial patterns, offering insight into the underlying neurobiology of gendered emotional phenomena.

Neurobiological Mechanisms

Neurobiology is the scientific study of the nervous system and its role in behavior and cognition, considered by some as a subdiscipline of both biology and psychology. A particularly active area over the past two decades has been the neurobiology of gender and behavior. Taking a biological approach, many researchers have sought to identify the mechanisms that give rise to gender differences in behavioral manifestations, from language to spatial performance to emotion. How does biology produce such differences? Even starting with the most simple manifestations of gender at birth, neurobiological mechanisms intervene. Almost all neurobiological mechanisms implicate the nervous system itself, and almost all neural processes are in turn influenced by hormonal secretions and genetic characteristics [1]. Following, the main sources of neurobiological differences between the sexes are briefly summarized.

The genetic blueprint of an organism is its fundamental biological mechanism; every other physiological property ultimately depends on this system. The genetic basis of biological sex—the presence or absence of a Y chromosome—is fundamental.

Steroid hormones act on the brain both during early development and later in adulthood, and their influences to some degree parallel gender differences in behavior.

Nearly every brain structure is affected by the presence or absence of genetic and hormonal sex factors. Areas frequently reported as different in adults include the hypothalamus, bed nucleus of the stria terminalis, amygdala, hippocampus, and corpus callosum. Sexual dimorphisms tend to be more prominent in the right hemisphere than the left, are most consistently observed in structures linked to reproduction, and are accompanied by differences in functional connectivity both within and between neurotransmitter systems.

Impact on Social Interactions

Gender bears on social interactions. Males and females differ generally in their preferences for competitive versus cooperative interactions, prioritize social goals in distinct ways, manifest stubbornness with different strategies and consequences, and confront explicit social guidance by adapting to norms or by rebelling. They also tend to differ in their sensitivity to social cues, with females often emphasizing rapport and males favoring status [1]. In behavioral cooperation experiments, dyads containing at least one male attained significantly higher performance than did female–female dyads. Individual males and females showed significant activation in the right frontopolar and right inferior prefrontal cortices, with this activation greater in females compared to males. Female–female dyads had significant inter-brain coherence within the right temporal cortex, whereas male–male dyads cohered in the right inferior prefrontal cortex. Mixed-sex dyads did not display significant coherence. Among same-sex dyads, inter-brain coherence positively correlated with cooperation performance. A frontal-temporal brain network underlies social cognition, involving sub-regions of the prefrontal cortex responsible for social value judgments and areas associated with person-centered social processing, including interpretation of biological motion, perception of bodily actions, theory of mind, and sense of agency [10].

Gender and Mental Health

Many neuropsychiatric illnesses occur more commonly in women, notably major depressive disorder and generalized anxiety disorder [11]. Responsible genes may present only on the X or Y chromosome or be expressed differently due to escape from X inactivation or epigenetic influences. Sex differences may exist in brain anatomy, circuitry, function, or output, causing the brain to be viewed not as dichotomous but as a mosaic of relative maleness and femaleness. Functional sex differences exist in the central nervous system, hypothalamic-pituitary-adrenal axis, and sympathetic-adrenal-medullary axis. Sex differences in the immune system, cardiovascular system, and gut exert influence on brain pathways. Gonadal hormones influence the human experience throughout life, especially during puberty, the menstrual cycle, pregnancy, the postpartum period, lactation, and menopause and through use of hormone-based contraceptives, hormone-replacement therapy at menopause, and fertility hormones in women, and through hormones used for gender-affirming care and treatment of transgender individuals. Adrenal androgens and estrogen both exert protective effects against affective and anxiety disorders. Both endogenous and exogenous gonadal hormones may influence treatment efficacy in women. Hormonal instability may, in itself, pose a risk to the mental health of women by destabilizing homeostasis.

Neuropsychiatric disorders with origins in development are differentially diagnosed in males. Attention-deficit/hyperactivity disorder and autism spectrum disorder occur more commonly in boys, whereas dyslexia and early-onset schizophrenia are more common in men [1]. Advances in elucidating the biological foundations of sex differences in the brain shed light on the potential source of male vulnerability. Heightened excitation and neuroinflammation may converge with environmental insult to increase risk of dysregulation in developing males relative to females. Sex differences in physiology and behavior are found at every stage of the lifespan, and can vary profoundly with age, experience, and context. Not all differences between the sexes manifest in the same way, and attention must be given to the contributing variables, the magnitude of the differences, and the relative importance to a particular condition or disease state.

Prevalence of Disorders

Many mental and neurodevelopmental disorders show robust sex differences in prevalence and expression. Early onset disorders such as autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD) and Tourette's syndrome as well as the rare childhood disorders dyslexia and specific language impairment are more frequently diagnosed in boys than in girls; ASD is diagnosed approximately four to five times more frequently in males. Men are also more likely to be diagnosed with schizophrenia while women are more likely to experience depression, anxiety and eating disorders. These observed differences cannot be solely explained by sex-specific exposures such as socialization or traumas. Genetic sex alongside in utero and postnatal effects of gonadal hormones organize injury responses manifested later in life. Genes involved in tissue injury, repair and response to stress show sexually dimorphic expression that can influence receptivity to trauma, at least in rodents and in adulthood. However, nearly all disorders exhibit changes in sex differences across development making a complex etiology that includes both biological and environmental influences [12].

People assigned female at birth have been shown to be at a relative disadvantage for recovery across a range of neurological insult situations including traumatic brain injuries, stroke and vascular disease. Following ischemic brain injury or stroke, women develop larger localized lesions than do men and experience higher mortality at least until 75 years of age. Female animals also develop greater infarct volumes following acute injury paradigms. Many neurodegenerative conditions such as Alzheimer's disease (AD) or Parkinson's disease (PD) show strong association with age, through the direction of the effect and whether it is a risk factor or protective varies between studies. Females are overall more susceptible to AD and men to PD while aging results in onset for both at risk sexes. Indeed, the symptoms associated with AD, including medial temporal and hippocampal atrophy, are more rapidly progressive in women than in men indicating a sex-dependent clinical trajectory for the disorder.

Not all sex biases are universal across age, however, with the relationship between sex and prevalence often showing reversals during development and aging: schizophrenia, for instance, exhibits more male than female patients prior to the age of 36 but appears slightly female-biased thereafter. Put another way, in pre-adolescents, boys are more vulnerable to a broad spectrum of neurodevelopmental disorders whereas girls are more vulnerable after puberty to disorders with later adolescent or adult onsets [1].

Neurobiological Underpinnings

Neurobiology is the study of how the nervous system develops, its structure, and the mechanisms by which it functions. It also addresses how the nervous system influences and is influenced by behavior and cognitive function. Different approaches include biological, cognitive, clinical, developmental, behavioral, molecular, computational, and evolutionary viewpoints.

Gender differences in behavior, cognition, and the brain have been studied for decades. The ways in which genetics, hormones, and the environment affect the brain contribute to establishing the brain's sexual differentiation and the foundation for sex-typical patterns of behavior. Relatively little is known about how the nervous system translates sexual differentiation into the expression of social behavior, but some of the neurons involved have been identified. Neuroanatomical and functional imaging studies identify sex differences in brain structure and function, which can also underlie the crossing of hormonal and genetic influence with environmental factors and experience. The interaction between the effects of organization and activation of the sex differences in the integration of behavior, cognition, and emotion underpin gender-specific patterns of both healthy and pathologic conditions.

The combined effects of genes, steroid hormones, and experience reach structural maturation before birth in many animal species. Gene expression is largely controlled through the effects of sex chromosomes and hormones, and notably, wherever the extent of gene expression is quantified, the large majority of sex differences are on the order of 2- to 6-fold. Minor differences clearly can produce major effects, but the activity of some master regulator genes—such as Sry in mammals or doublesex in insects—simultaneously induces the expression of many other genes, which can amplify the effect many-fold. The same hormones and signals responsible for defining sexual identity and even gonadal development have direct neural effects. Specific processes in the brain that appear to be widely affected are synaptogenesis and neuronal survival, and organized patterns of behavior can be reversed by relatively small amounts of hormone at specific times. This results in the possibility that only limited numbers of targets accumulate sexual dimorphism, even while many others modulate or respond to these targets. Animal and human studies suggest the spinal cord and the hypothalamus—both of which have known roles in reproduction and generate a relative abundance of the identified behaviorally critical targets—may be within this category [1].

Impact of Environment on Gender Behavior

Culture influences contemporary behaviors with gender-related attributes [13]. It encourages different developmental pathways in boys and girls, with males typically showing a greater inclination for rough-and-tumble play and an earlier preference for vehicles and wheeled toys, whereas females favor nurturing play and preferring dolls and similar objects. However, natural differences are superimposed on any cultural factors, and it is ill-advised to interpret all sex differences in behavior as the result of socialization. The brain shows complex responses to environmental cues that depend on biological sex, and the developing endocrine environment defines a range of sex-specific neurophysiological states to which experience is applied. The interaction between genes and environment is crucial for shaping anatomical and physiological circuits, but the extent to which neural substrates of behavior retain plasticity at later development stages is still unresolved.

Cultural Influences

Social and cultural environments influence the neurobiology that guides gendered behaviour. Cultural expectations and shared norms shape social interactions and provide opportunities for communication, collaboration, and sometimes conflict through the expression of gender-related behaviours. Through extensive interactions among networks of individuals, cultures develop dominant social structures that govern the actions of members within those societies. Cultural variations lead to behavioural differences at the individual level, predisposing many species to demonstrate a template of social behaviour that appears preferentially in groups of the same species [1]. Humans, fish, birds, and primates exhibit cultural patterns of behavioural processes that influence social interaction and other psycho-social behaviors [14].

The human female brain contains a region of tissue with microstructure that is differently organized when compared with that of both females and males. A small nucleus in the mouse brain contains many more neurones in females than in males, thus reversing the pattern that has been observed in every other sexually dimorphic brain regions examined. Genetic and endocrine factors regulate the regional development of brain sex differences, but differences in cell birth, death, migration and differentiation are unlikely to account for this reversal, suggesting that considerable diversity exists in the ways the sexual differentiation of brain and behaviour is achieved.

Developmental Factors

Early studies theorized that Gender Identity Disorder (GID; now Gender Dysphoria) develops from the interaction of genetics, brain development, and culture. Neural plasticity, hormone effects, and brain structure differences are involved in gender identity development [13]. Genetic effects remain to be firmly established [15]. Pre- and postnatal environmental, biological, cognitive, and socio-cultural factors influence the developing capacity to behave in ways culturally assigned to males or females. In many species, early life experience interacts with the sexually dimorphic brain to influence subsequent gender-role behavior [1]. Gender development is not fixed at birth and alters brain, body, and behavior throughout life.

Neuroplasticity and Gender Behavior

Sex-based distinctions in the brain underlie numerous gender-specific behaviors, but the neurobiological mechanisms that allow for changes in these behaviors are still not fully comprehended. The differences in neural circuit structures typically emerge at birth, influenced by both genetic makeup and hormone interactions during critical developmental windows. These foundational setups create the groundwork for reproductive methods and social functions. Following this, brain plasticity enables modifications in phenotype to adapt to environmental conditions, facilitating adaptability in reproductive strategies within either sex or gender. For instance, the SBN nodes that represent reproductive strategies in an animal subjected to [1-16] a dominant social environment can be configured very differently from those that emerge in a subordinate individual. Plasticity continues to shape the brain well into adult life: it is now widely accepted that the exquisite sensitivity of the nervous system to environmental modulations declines across the lifespan but does not end at puberty.

Cultural crawling also plays a major role in the initial mapping of the brain as individuals recruit social cues to guide developmental trajectories across the system. The use of compulsory heterosexuality and the duty to forge psychologically coherent gender identities constitute fundamental drives that impose themselves very early on the control of behaviour. Normative social expectations supply both the content and frameworks of reference within which individuals learn to commit themselves to one or another gender. Psychiatric consciousness therefore develops in response to an algorithm of social forces and remains channelled by it in adulthood. The psychological loop that results operates on multiple temporal scales—past and present, collective and individual, upstream and downstream—to sustain a series of interlocking cycles of conceptual closure within which there remains effectively no possibility of escape.

Research Methodologies in Gender Neurobiology

The neurobiological bases of gender differences are approached via neuroimaging and behavioural techniques [17]. The review discusses how MR technology can be deployed, the behavioural tests adapted, and the experimental protocols used to investigate the psychobiological components of human gender. It concludes with two examples that highlight the indispensability of these complements to better understand gender, identity, and behaviour.

In the field, MR technology provides valuable techniques for noninvasive in vivo study of anatomical, structural, and functional characteristics of the brain. These techniques enable detection of anatomical differences, defining structural and functional connectivity, measure heart rate, respiratory rate, facial temperature, and employ eye-tracking, which collectively allow exploration of expressive behavioural dynamics under diverse biological and pyschosocial contexts. Eye movement can be related to decision-making processes and might be used to detect cognitive processes related to facial recognition of emotions and affective processing. Behavioural assessments are widely used and provide information about levels of alertness, psychomotor activity, stress, memory devices, schedules, eating behaviours, social capabilities, and other functions that can be linked to neural activity measured with MR devices. Questionnaires are also used to provide insight into psychological states and were instrumental in obtaining responses from gender-diverse subjects who did not want to be recorded through visual behavioural techniques.

Behavioural and neuroimaging techniques are complementary methods for a multidisciplinary approach to psychological and physiosocial studies of gender. MR techniques enable a wide range of analyses of anatomical, structural, functional, cognitive, and emotional characteristics, allowing investigations of sex/gender differences, sexual orientation, and gender identity conditions. Behavioural techniques provide a characterization of a subject's psychological state, emotional and cognitive processing, sociocultural encounters and constraints, and contribution to the social construction of human gender. Cross-disciplinary studies of human gender must incorporate both types of techniques to achieve a comprehensive overview. Experiment design should integrate MR, behavioural, and psychological components into a single unified protocol to enhance the validity of investigations and serve as a robust methodological framework for advancing theory and knowledge of human gender neurobiology.

Neuroimaging Techniques

Modern neuroimaging systems are capable of capturing brain dynamics with multiple imaging modes in the frequency band approximately 0–10 kHz. This multi-modal capability enables accurate measurements over a wide frequency range for spatially distributed brain activity while remaining portable and practical. Three widely applied neuroimaging techniques—magnetoencephalography (MEG), electroencephalography (EEG), and functional magnetic resonance imaging (fMRI)—offer crucial insights into the neurobiology of gender and behavior. fMRI directly measures brain activity by detecting small signal changes reflecting regional hemodynamic response, which correlates well with underlying neural activity. MEG and EEG detect the coherent magnetic and electrical signals, respectively, produced by synaptic activities in neuron populations; these methods provide superior temporal resolution, capturing sub-millisecond brain dynamics. High-density EEG systems, with up to 512 sensors, offer enhanced spatial resolution. Combining these techniques—leveraging the high spatial accuracy of fMRI with the exquisite temporal precision of MEG/EEG—enables detailed investigation of a wide frequency range of brain dynamics.

Behavioral Assessments

The neurobiological approach to assessing behavior continues to be translated into animal paradigms that explore the underlying mechanisms. Such assessments have been especially informative in clarifying the interplay of gender and behavioral traits [18]. Behavioral models used to assess species-typical and pathological behaviors can be incorporated into paradigms with pharmacological or physiological manipulations in a wide range of species, from fish and amphibian species to rodents, primates, and humans. A common set of well-validated behavioral paradigms has been developed, including assessments of exploration and activity, anxiety, sensorimotor gating, attention, approach/avoidance, risk-taking, social interaction, olfactory function, spatial learning, and other processes [19]. Typically, these tasks have been combined into test batteries to provide efficient phenotypic screens and time-dependent analyses of behavioral responses. These models demonstrate that many sex differences in behavior emerge before puberty, showing that the primary causal factors are not the gonadal steroid hormones whose release increases at that time, but rather other influences such as gonadal steroid and sex chromosome actions during earlier developmental stages.

Case Studies in Gender and Behavior

Gender identity, defined as an individual's sense of being male or female, typically forms in childhood and is often congruent with one's biological sex [15]. While gender identity normally develops along these lines, cases of identification with the opposite gender or feelings of belonging to a different gender altogether are observed prior to adolescence. Fulfilling roles associated with the opposite gender, particularly when such identities cause significant distress as seen in transsexualism (now more commonly referred to as gender dysphoria), is documented. Sexual orientation among transsexuals varies, ranging from attraction to the acquired gender, to the bi- and asexual orientation. Understanding the underlying functions of the brain requires detailed examination of neuroanatomy and neurophysiology to identify characteristics reflecting genetic and endocrine sex differentiation. Neuroanatomical investigations of male-to-female and female-to-male transsexuals are particularly valuable, though the preservation of the gender identity of female-to-male transsexuals into old age provides the most studied clinical sample.

The influence of sex hormones on behavior shapes developmental trajectories and appears to reflect neuroanatomical organization. These aspects are instrumental in understanding the neurobiology of gender-based behavior and identity.

Brain circuitry in intersexed individuals categorically deviates from the sexual dimorphism observed between typical male and female brains. Collected data indicate a closer affinity of transsexual brains to their preferred gender rather than to their biological sex, with an exception noted in female-to-male transsexuals. This discrepancy underscores the complexity of gender-related brain differentiation and its behavioral manifestations.

Transgender Individuals

Differences in a variety of brain systems between male- and female-typical populations have both direct and indirect roles in mediating aspects of sex-typed and gendered behavior. Differences in the prevalence rates of particular somatic and psychiatric illnesses between men and women, such as depression and anxiety disorders, are similarly linked to the observed structural sexual dimorphisms in brain anatomy and functional organization.

The hypothesis that brains of transgender women are shifted away from their biological sex towards their gender identity received further support from studies on the structural connectivity network. A combined analysis of behavioral measures and structural connectivity showed which brain systems remain most closely aligned with gender identity, an important insight into transsexualism and potential mechanisms underlying the perception of internal body consciousness [5]. Cross-sex hormone treatment changes own-body perception in gender dysphoria, with differences in behavior and brain connectivity profiles that illuminate the development of a clinical marker and offer insights into underlying mechanisms [20].

Intersex Conditions

Variations in sexual development produce intersex conditions that demonstrate the heterogeneous processes underlying sexual differentiation and contribute to the broader understanding of gender development [21]. True hermaphroditism, the only documented case of ovotesticular intersexuality, presents with both ovarian and testicular tissue, typically bilaterally or on opposite sides within the same gonad. Genitourinary complicity is a common feature in nearly all intersex syndromes. Therefore, extensive prenatal and subsequent medical examinations of neonates exhibiting genital irregularities play a pivotal role in accurately understanding the neurobiology of intersex individuals.

Ethical Considerations in Research

The history of scientific study of gender and behaviour is rife with bias, and attempts to understand the biological basis of gender carry substantial ethical weight. Although the neurobiological underpinnings of gender are an important and intriguing area for research, the researcher must be acutely sensitive to the social consequences of interpretation, and must be vigilant about the dangers of examining new data for preconceived evidence.

Inclusion of females in neuroscience is increasing but the literature remains male biased, and many authors do not document or justify the sex of experimental animals [21]. When a transdisciplinary framework is adopted, the analysis of results for preferential, direct, or causal sex/gender relations only makes sense if a clear a priori hypothesis exists, if the investigation of a possible direct cause is justified, or if the sample clearly paves the way for specific group comparisons of interest [22]. Even when no clear hypothesis exists, large datasets with many large groups may be well suited for exploratory (data-driven) analyses. When interpreting any sex/gender differences, researchers should also consider the full biopsychosocial complexity of the topic and be wary of oversimplification.

Sex differences in dopaminergic function in the striatum and nucleus accumbens, and the effects of oestrogen on dopaminergic activity, have substantial implications for the neurobiology of psychosis-related behaviour, which are also modulated by gender in humans [23]. Sex differences also affect drug abuse and therefore raise important ethical questions about experimental design. The neurobiology of psychosis is therefore a useful model for discussing the consequences of sex and gender for both scientific methodology and ethical considerations.

Future Directions in Neurobiology of Gender

Neurobiology addresses the biological basis and function of neurons. At its inception, behavioral endocrinologists associated sex differences in behavior with somatic characteristics such as genitalia or plumage. This mechanistic view that the brain simply executes fixed action patterns was challenged by findings from guinea-pig experiments: pregnant animals treated with testosterone produced daughters exhibiting male-typical copulatory behaviors, implicating social hormones as agents of brain organization rather than the body. Subsequent discoveries revealed structural brain differences, including a sexually dimorphic song-control nucleus in zebra finches and a larger preoptic nucleus in male rodents, supporting the presence of neural substrates that regulate sex differences. The 1980s extended these findings by linking brain structures to sexual orientation; for instance, a hypothalamic nucleus found to be larger in heterosexual than homosexual men. Despite these advances, sex differences in the brain remained largely interpreted within a reproductive framework, consistent with the dominance of neuroendocrinology at the time. A later widespread shift to males in hippocampal physiology research can be attributed to the observation that dendritic spine density fluctuates across the estrous cycle in females. Today, a growing recognition of a gender bias in neuropsychiatric and neurological disorders, combined with supportive institutional policies, underpins a renewed interest in the significance of neurobiological sex differences [1].

Continued inquiry into the relation between brain and behavior has converged on three principal research strategies: (a) comparing the neuroanatomy of males and females across species to identify developmentally important structures; (b) demonstrating that sex differences in reproductive behavior require the presence of sex differences in the brain, thereby providing a physiological context; and (c) investigating the influence of sex chromosomes on traits such as reproductive maturation, cognitive function, disease susceptibility, and brain morphology. Methods geared towards characterizing these effects have been grouped into three categories: (a) dose and receptor manipulations of different hormones and/or receptors, applied prenatally, perinatally, postnatally, or at other developmental stages; (b) various manipulations and comparisons of sex chromosomes, including studies of individuals with sex-chromosome aneuploidies or sex-reversal, the creation of chimeras, or investigations involving specific genes on the Y or X chromosome; and (c) analyses of environmental and social factors—such as exercise, housing, social interactions, sex, age, parental care, enrichment, and stress—and their organizational neural effects [15].

Looking forward, interdisciplinary approaches that integrate sensitive clinical assessments, cutting-edge neuroimaging and genetic technologies, and appropriately designed varied paradigms hold promise for clarifying interactions between gender, the brain, and complex behavioral patterns.

Emerging Technologies

Research on the neurobiology of gender is increasing. A flourish of technology provides powerful windows for scientific renewal. The second act of the story is complex and calling for an audience. One Technology Can Foster Foresight. A flood of new isotopic-ratio measurements, combined with large data compilations of uranium "box" models, has recently flooded the uranium-isotope literature and inspired consideration of the subtle links between uranium isotopes and global climate. Oceanographers say ion microprobe–based measurements of U isotope ratios—by permitting a retrieval of the past oceanic oxygen budget—open an entirely new window on the nature of the Proterozoic world, enhancing current capability to investigate climate forcing and atmospheric development on the early Earth [1]. The form of this data has already impressed researchers who search for trace element proxies of Earth evolution, especially if the same anomalous lower mantle, high-temperature REE mix can be seen in both the trace element and isotopic data. Another Strategy to Tackle the Unknown. An informed, tightly linked interdisciplinary strategy would have undermined, ahead of time, nuclear winter's original geomorphic assumptions, nuclear war's ignition energy, thermal pulse models, and photochemical-kinetics analyses.

Interdisciplinary Approaches

Coordinated inquiry is necessary to understand the neurobiological mechanisms by which sex and gender affect behavior and mental health [15]. Gynecology and the behavioral sciences suggest a range of starting points for investigating those mechanisms. As an interdisciplinary endeavor, neurobiological research on sex and gender is fertile ground both for application of existing neurobiological techniques and for development of new methods that could aid basic dissection of the brain's behavioral functions.

Associations between gonadal secretions and the development and expression of behavior provide a natural starting point, and much is known about each. Established behavioral neuroendocrinology methods can be adapted to investigate sex-specific hormones and behaviors, and new, more specific tools can build on these capabilities. The rapid rise of immunohistochemistry during the 1980s and 1990s is one example: extensive behavioral research involving the stress hormone glucocorticoid was done alongside the development of an antibody that participates in the stress response, a manufactured reagent that became the most widely used single test for stress. Because the hormone was well characterized, researchers were able to fine-tune the antibody's binding properties and to work with the antibody and other already-established reagents for modulation of stress hormones, a perfect confluence of needs, opportunity, and available techniques. Consequently, junctures between behavioral and physiological sex differences have been particularly productive areas for research, and the development of specific research tools should be viewed as an urgently needed parallel.

Reproductive behaviors come into play in a wide range of disciplines. Early in biological research, sexual dimorphism was widely accepted in mammals; general anatomical investigations incorporated sexual dimorphism routinely [1]. While sexual dimorphism in the brain was known through 20th-century research with middle- to large-brained animals, only the more detailed characterization of extraordinarily large sex differences in reptiles drew widespread attention to the brain. Maternal care is another class of behaviors investigated in many contexts, from pediatric psychiatry to behavioral pharmacology. Investigations of swarming, mating, and nesting of every kind, both internal and external, are equally common, and numerous other transitions [e.g., puberty, pregnancy, and menopause] link to hormone and behavioral research.

Final Thoughts and Conclusion

Gender differences have intrigued neurobiologists for decades. The field is now mature enough to conclude with some confidence that scientific investigation of these differences can explain, in part, why women on average—globally, across racial and cultural divides—tend to be one way and men another. Many of the behavioral differences commonly ascribed to cultural influences are probably driven at least partly by biology. The biological influences are critical enough that when a person alters their gender-role behavior permanently and dramatically, their brain changes permanently and dramatically as well. Gender is governed through multiple mechanisms—including genetics, sex hormones, many facets of brain anatomy, several specific cognitive characteristics, numerous attributes of emotional processing, particular patterns of mental illness—and biological drive appears present in both the prenatal and postnatal environment. These biological influences are mapped onto behavior through complex culture-bound systems that are nevertheless shaped by basic fundamental neurobiology [1]. Success at creating scientific explanations of behavior may require a more forceful reliance on the neurobiology of gender.

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