Editorial Article ISSN 2693-2504

Journal of Bioscience & Biomedical Engineering

Brain–Sex Differentiation: Biology, Time, and the Aging Brain

Dr. Divya. R

Professor of Physiology, Trichy SRM Medical College Hospital & Hospital, Trichy, Tamilnadu, India.

***Correspondence authors**

Dr. Divya. R,
Professor of Physiology, Trichy SRM Medical College Hospital & Hospital, Trichy, Tamilnadu,
India.

Submitted: 26 Jan 2026; **Accepted:** 2 Feb 2026; **Published:** 10 Feb 2025

Citation : Divya, R. (2026). Brain–Sex Differentiation: Biology, Time, and the Aging Brain. *J B & Bio Engine 6*(1): 1-2.
DOI : https://doi.org/10.47485/2693-2504.1060

Neuroscience has long been fascinated by the question of how sex-related differences emerge in the human brain, not because the answers are simple, but because they consistently reveal complexity rather than clarity (Hall & Hall, 2020). Brain–sex differentiation refers to a set of biological processes through which neural structure and function are shaped by genetic signals, hormonal environments, and developmental timing (Barrett et al., 2019). This process must be carefully distinguished from gonadal sex and from gender identity, both of which follow different biological and psychosocial trajectories (Carlson & Birkett, 2021).

The earliest influences on brain–sex differentiation arise at the level of chromosomes, where genetic sex is established at fertilization (Barrett et al., 2019). The presence of the Y chromosome, through expression of the SRY gene, initiates testicular development and alters the fetal hormonal milieu (Hall & Hall, 2020). In contrast, the absence of SRY permits ovarian differentiation, resulting in a fundamentally different endocrine environment during brain development (Koeppen & Stanton, 2017). Beyond their role in gonadal formation, sex chromosomes themselves exert direct effects on neural cells, suggesting that genetic influences on the brain extend beyond hormone mediation (Kandel et al., 2021).

Hormonal organization of the brain during prenatal and early postnatal life represents a pivotal phase in sex-related neural differentiation (Hall & Hall, 2020). During critical developmental windows, testosterone secreted by the fetal testes enters the brain and is often converted locally to estradiol by aromatase (Barrett et al., 2019). This estradiol acts on developing neurons to influence survival, connectivity, and synaptic patterning (Carlson & Birkett, 2021). Such organizational effects are enduring, establishing neural architectures that persist long after the hormonal signals themselves have subsided (Koeppen & Stanton, 2017).

Certain brain regions show consistent average differences related to these developmental processes (Kandel et al., 2021). The sexually dimorphic nucleus of the preoptic area has been extensively studied for its size differences and association with reproductive behaviors (Carlson & Birkett, 2021). Other regions, including the bed nucleus of the stria terminalis, amygdala, and hippocampus, also demonstrate sex-related variation in structure and connectivity (Bear et al., 2015). These findings, however, describe trends across populations and should not be interpreted as defining features of individual brains (Bear et al., 2015).

At the cellular level, sex steroids influence neurodevelopment by regulating apoptosis, neurite outgrowth, and synapse formation (Kandel et al., 2021).
They also modulate major neurotransmitter systems, shaping inhibitory and excitatory balance within developing circuits (Carlson & Birkett, 2021). Increasing attention has been directed toward epigenetic mechanisms, through which hormones produce long-lasting effects by altering gene expression without changing DNA sequence (Kandel et al., 2021).

Brain–sex differentiation does not end with early development but continues to be shaped by hormonal activity across the lifespan (Hall & Hall, 2020). Puberty represents a second major period during which circulating sex steroids activate previously organized neural circuits (Barrett et al., 2019). Unlike organizational effects, these activational influences are dynamic and reversible, reflecting ongoing endocrine states (Koeppen & Stanton, 2017).

The relevance of brain–sex differentiation becomes particularly apparent when viewed through the lens of aging (Kandel et al., 2021). Age-related declines in estrogen and testosterone are associated with alterations in synaptic plasticity, cognitive function, and emotional regulation (Barrett et al., 2019).
Epidemiological and clinical studies consistently report sex differences in the prevalence and progression of neurodegenerative disorders (Bear et al., 2015). These patterns likely reflect the cumulative impact of lifelong interactions between hormones, neural circuits, and genetic susceptibility (Kandel et al., 2021).

Perhaps the most consequential implication of brain–sex differentiation research is not what it reveals about difference, but what it exposes about the limits of binary thinking in

biology (Carlson & Birkett, 2021).

As neuroscience moves deeper into the era of large datasets, lifespan imaging, and molecular resolution, it becomes increasingly clear that sex-related patterns in the brain are statistical tendencies rather than biological destinies (Bear et al., 2015).

Clinging to rigid classifications risks obscuring clinically relevant variability, particularly in aging populations where hormonal trajectories, life experiences, and disease processes diverge widely within each sex (Kandel et al., 2021). A more integrative framework—one that recognizes the brain as a dynamic, mosaic system shaped by time—offers a better foundation for understanding vulnerability, resilience, and therapeutic response in later life (Carlson & Birkett, 2021). In this sense, brain–sex differentiation should be viewed not as a tool for categorization, but as a lens through which neuroscience can approach aging with greater precision, humility, and care (Hall & Hall, 2020).

References

1. Hall, J. E., & Hall, M. E. (2020). Guyton and Hall Textbook of Medical Physiology (14th edition). Philadelphia: Elsevier. https://shop.elsevier.com/books/guyton-and-hall-textbook-of-medical-physiology/hall/978-0-323-59712-8
2. Barrett, K. E., Barman, S. M., Yuan, J., & Brooks, H. L. (2019). Ganong's Review of Medical Physiology (26th edition). New York: McGraw-Hill. https://www.amazon.in/Ganongs-Review-Medical-Physiology-26e/dp/1260566668
3. Carlson, N. R., & Birkett, M. A. (2021). Physiology of Behavior (13th edition). Boston: Pearson. https://books.google.co.in/books/about/Physiology_of_Behavior_Global_Edition.html?id=B_NWEAAAQBAJ&redir_esc=y
4. Koeppen, B. M., & Stanton, B. A. (2017). Berne and Levy Physiology E-Book (7th edition). Philadelphia: Elsevier. https://books.google.co.in/books/about/Berne_and_Levy_Physiology_E_Book.html?id=20IHDgAAQBAJ&redir_esc=y
5. Kandel, E. R., Koester, J. D., Mack, S. H., & Siegelbaum, S. A. (2021). Principles of Neural Science (6th edition). New York: McGraw-Hill. https://www.amazon.in/Principles-Neural-Science-MEDICAL-DENISTRY/dp/1259642232
6. Bear, M. F., Connors, B. W., & Paradiso, M. A. (2015). Neuroscience: Exploring the Brain (4th edition). Philadelphia: Jones & Bartlett Learning. https://www.amazon.in/Neuroscience-Exploring-Mark-F-Bear/dp/078177817

Copyright: ©2026. Divya. R. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.