Gender-specific differences in brain structure and function observed throughout the development are believed to contribute to differences in behavior, cognition, and the presentation of neurodevelopmental disorders. Although limited research is focused on this topic, mainly on changes in the levels of gonadal hormones early in gestation and differences in brain structure apparent at birth, the last decades of neuroscience research have provided considerable evidence that gender-specific differences in the brain are found at all levels of neuroscience. At the molecular and cellular level, brain sexual dimorphism has been observed in neural processes such as neurogenesis, cell growth, migration, formation of synapses, expression of receptors, apoptosis, and plasticity. The most recent study from American researchers has confirmed the results of some previous works which demonstrated that gender differences in functional brain connectivity are present *in utero.*

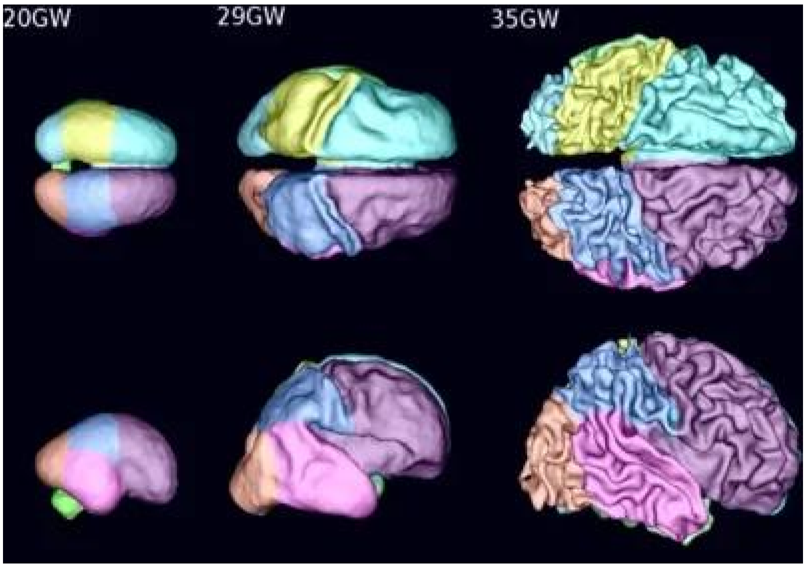
For the most part, gender-related brain dimorphism results from a cascade of events, beginning with the role of the gender-determining genes and continuing with the actions of gonadal hormones in embryonic, neonatal, peripubertal, and adult life. A critical period for the organizational effects of testosterone on brain structure in humans is thought to be from eight to 24 weeks of gestation. Testosterone acts to masculinize and defeminize the circuitry of the male brain. In contrast, a female phenotype develops in the absence of the androgenic hormones of the testes. Thus, estrogen actions in the female brain activate the functions that have been allowed to develop in the absence of testosterone.

*Neuroimaging studies*

Numerous neuroimaging studies demonstrated gender-specific differences at the structural and functional level: in the complexity and thickness of the brain cortex and the connectivity between brain areas. In their pioneering volumetric analysis of the fetal brains, DeLacoste et al. (1991) showed a greater weight of the right hemisphere in the male brains and a greater weight of the left hemisphere in the female brains. These findings were consistent with the original theory of cerebral lateralization of Geschwind and Galaburda (1987), who stated that a smaller left hemisphere is one of the consequences of higher testosterone levels found *in utero*.

In 2014, the magnetic resonance imaging (MRI) study of Li *et al*. provided evidence of significant gender-related dimorphism of the cortical structural asymmetry in newborns. They found a more prominent asymmetry of sulcal depth around the *planum temporale* and superior temporal sulcus in males than in females. In their later article, Wheelock et al. (2019) used the resting-state functional MRI (fMRI) to explore, for the first time, the gender-specific differences in the functional connectivity within and between networks in 118 human fetuses across the gestation. They found that early in gestation (between 25 and 38 weeks), the female fetuses had a greater change in long-range functional connectivity, while the male fetuses exhibited a greater change in local functional connectivity and confirmed that gender differences in brain connectivity are present *in utero*.

In 2014, the diffusion tensor imaging (DTI) method used by Ingalhalikar and associates to assess human connectome in a large population of 949 young people aged 8 to 22 years demonstrated fundamental gender-specific differences in the structural architecture of the human brain. The most pronounced gender-specific differences were registered in the adolescent brains (aged 13.4 to 17 years), indicating an early separation of the developmental trajectories between the genders. The males had a higher within-hemispheric connectivity ratio in the frontal, temporal, and parietal lobes bilaterally. The modularity and transitivity were higher in males compared to females. The female brains showed higher inter-hemispheric connectivity and greater across-lobe connectivity, mainly between the lobes in different hemispheres. According to the authors, men’s brains are optimized for communication within the hemispheres, while women’s brains are optimized for interhemispheric communication.




***About the study***

In this study, the research team performed resting state fMRI on 95 human fetuses between 19 and 40 weeks of gestation. The pattern of functional brain connectivity successfully classified fetal gender with 73% accuracy. Highly consistent predictors included connections in the somatomotor and frontal areas alongside the hippocampus, cerebellum, and basal ganglia. High consistency features implicated a greater magnitude of interregional connections in females, while male-weighted features were predominately within anatomically bounded regions.

These findings revealed that fundamental differences in the human connectome specific to gender are present and reliably detectable even before birth. These results are consistent with the fMRI study of Wheelock et al. (2019) who discovered that early in gestation (between 25 and 38 weeks), the female fetuses showed greater change in long-range functional connectivity, while the male fetuses exhibited a greater change in local functional connectivity. Also, these results are in line with the abovementioned DTI study by Ingalhalikar *et al.* conducted in adolescents which showed higher inter-hemispheric connectivity and greater across-lobe connectivity, mainly between the lobes in different hemispheres in female brains, whereas males had a higher within-hemispheric connectivity ratio in the frontal, temporal, and parietal lobes bilaterally.

The study findings were published in the Cerebral Cortex.

*Journal Reference*

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