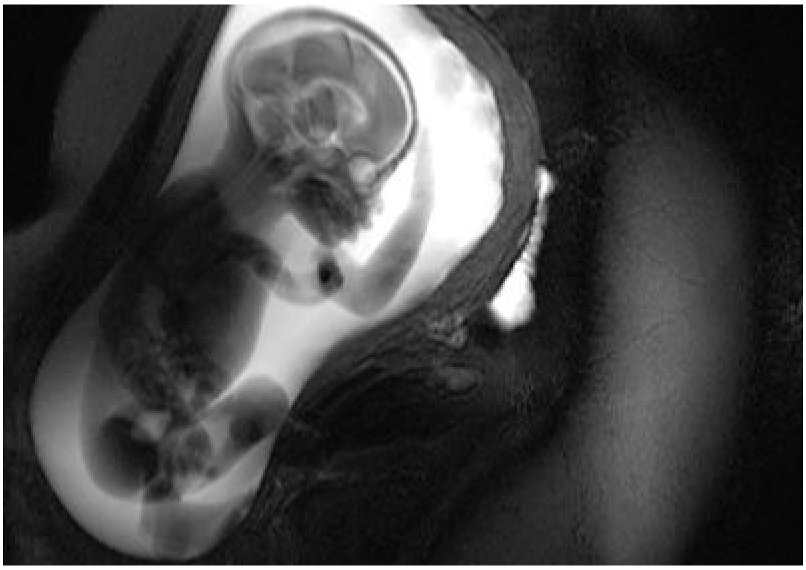
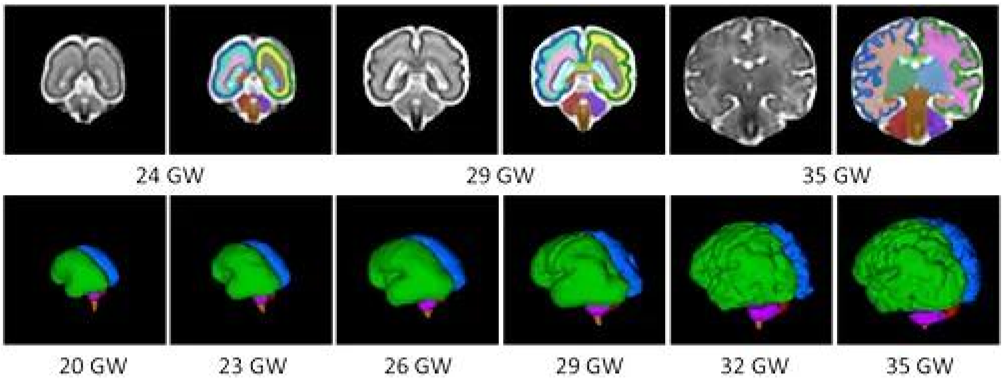
The last decades of neuroscience research provided considerable evidence that sex-specific differences exist at all levels of neuroscience. At the molecular and cellular level, brain sexual dimorphism has been observed in neural processes such as neurogenesis, cell growth, migration, formation of synapses, expression of receptors, apoptosis, and plasticity. In a new study, American researchers have used resting-state functional magnetic resonance imaging (fMRI) to identify sex-specific differences in brain functional connectivity *in utero*.



In their pioneering volumetric analysis of the fetal brains, DeLacoste et al. (1991) demonstrated 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 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 *in utero*. In 2014, Li et al. used MRI in newborns and provided evidence of significant sex-related dimorphism of their cortical structural asymmetry. They observed more prominent asymmetries of sulcal depth around the *planum temporale* and superior temporal sulcus in males than in females.



In 2014, the diffusion tensor imaging study of Ingalhalikar et al. assessed the connectome in a large population of 949 young people aged 8 to 22 years. The findings revealed fundamental sex-specific differences in the structural architecture of the human brain. The results demonstrated a higher within-hemispheric connectivity ratio in the frontal, temporal, and parietal lobes bilaterally in males. However, the female brains tend to show higher inter-hemispheric connectivity and greater across-lobe connectivity, mainly between the lobes in different hemispheres. The modularity and transitivity were higher in males compared to females.

Importantly, the most pronounced sex-specific differences were observed in the brains of adolescents (aged 13.4 to 17 years), indicating an early separation of the developmental trajectories between the genders. The authors postulated that men's brains are optimized for communication within the hemispheres, while women's brains are optimized for interhemispheric communication.

In 2019, the resting-state fMRI study of Wheelock et al. explored, for the first time, the sex-specific differences in the functional connectivity within and between networks in 118 human fetuses *in utero*. The findings revealed that during early gestation (between 25 and 38 gestation weeks) greater changes in long-range functional connectivity were present in the female fetuses. At the same gestation time, male fetuses had greater changes in the local functional connectivity.

About the Study and Results

The research team used resting state fMRI scans of 95 human fetuses, performed between 19 and 40 weeks of gestation. The findings showed that functional brain connectivity patterns classified fetal sex with an accuracy of 73%. The researchers identified features (functional connections) that reliably differentiated fetal sex. Highly consistent predictors included connections in the somatomotor and frontal cortical areas alongside the hippocampus, cerebellum, and basal ganglia. Furthermore, whilst male-weighted features were primarily found within anatomically bounded regions, high-consistency features suggested a larger magnitude of interregional connections in females.

These findings of sex-specific differences in brain functional connectivity *in utero* are consistent with findings of greater changes in long-range functional connectivity in female fetuses, described in the resting-state fMRI study of Wheelock et al (2019), as well as with fundamental sex-specific differences in brain functional connectivity during adolescence, found in the study of Ingalhalikar et al (2014).

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Journal Reference

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