

Research on human brain development sheds light on neurodevelopmental disorders

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New research from the Institute of Psychiatry, Psychology & Neuroscience (IoPPN) at King's College London has found that some processes behind the early development of GABAergic neurons, neurons that produce the main inhibitory chemical messenger in the central nervous system, are consistent between humans and mice.

The research, published in *Science*, is a collaboration between King's

IoPPN and several Chinese institutions. It is the first thorough investigation of human interneuron development and has clarified important similarities and differences between human and mouse [brain development](#).

Understanding the mechanisms that control the generation of human cortical GABAergic interneurons has important implications for human health. Neurodevelopmental conditions such as autism and schizophrenia are caused, at least in part, by genetic variation, as genetic changes result in increased susceptibility to these disorders by affecting how specific cell types develop.

The investigators used single cell RNA sequencing to delineate the emergence of cell diversity in the ganglionic eminences—the region of origin of GABAergic interneurons. In doing so, they discovered remarkable consistency between the early developmental processes in the brains of mice and humans.

The sequencing allowed Professor Oscar Marin of King's IoPPN and his colleagues to construct spatial and temporal maps of gene expression through the early second trimester of human development (equivalent to weeks 9-18 of the gestational period).

The organization and cellular architecture of the telencephalon, the largest and most developed part of the brain, is broadly conserved between mammals although both its size and complexity vary enormously between rodents and primates. Previous analyses have shown that the cells making up the cerebral cortex are relatively similar between mice and humans. However, extensive differences exist in the relative proportions, tissue distribution, and gene expression patterns of specific types of interneurons in the adult brains of mice and humans.

Professor Marin, Head of Department of Developmental Neurobiology

at King's IoPPN said that "this work elucidates the emergence of human GABAergic neurons and defines the commonalities and differences between us and rodents. Importantly, our work enables new levels of understanding of neurodevelopmental disorders. Many of these disorders have overlapping genetics and phenotypes and changes in striatal and cortical GABAergic neurons have been robustly documented in both autism and schizophrenia."

The researchers now hope that this work will enable other research to link gene variation and cell types in neurodevelopmental disorders, resulting in new insights and new avenues for individualized therapies.

More information: Yingchao Shi et al, Mouse and human share conserved transcriptional programs for interneuron development, *Science* (2021). [DOI: 10.1126/science.abj6641](https://doi.org/10.1126/science.abj6641)

Provided by King's College London

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