

Genes sow seeds of neuropsychiatric diseases before birth, in early childhood

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A depiction of the double helical structure of DNA. Its four coding units (A, T, C, G) are color-coded in pink, orange, purple and yellow. Credit: NHGRI

From early prenatal development through childhood, the prefrontal cortex of the human brain undergoes an avalanche of developmental activity. In some cases, it also contains seeds of neuropsychiatric illnesses such as autism spectrum disorder and schizophrenia, according to a new genetic analysis led by researchers at Yale University and the University of California-San Francisco (UCSF).

Previous studies have identified DNA variants linked to neuropsychiatric illnesses, but it has been unclear just when those variations might trigger functional changes in the dorsal lateral prefrontal cortex, a region closely linked to neuropsychiatric, cognitive, and emotional disorders. This new study, published April 7 in the journal *Cell Reports*, added a new dimension to prior research. The scientists also measured the amount of RNA, which provides a picture of overall gene activity, in 176 [tissue samples](#) across a variety of developmental stages to determine how and when DNA variants influence brain function.

"This is the first large cohort to profile DNA and RNA both in prenatal and postnatal human brain samples, making it an unprecedented resource for understanding how individual genetic differences might lead to functional differences," said Yale's Sirisha Pochareddy, an associate research scientist in neuroscience and co-lead author of the study.

Understanding how genetic variation and changes in function are linked will help scientists understand how alterations of brain development can lead to schizophrenia and autism later in life, said the authors of the study. Since the research tracked thousands of variants associated with thousands of genes across the [entire genome](#), scientists can identify groups of genes that regulate distinct biological processes and study how they can lead to disease, they said.

"Human brain development is an incredibly complex and dynamic process, and any disruption along the way can have profound

consequences on later brain function," said co-lead author Donna Werling, formerly of UCSF and now at the University of Wisconsin-Madison. "Interestingly, we found that some genetic variants have stronger effects on RNA expression before birth and other variants with strongest effects after birth."

Studying these age-specific effects can open more doors for learning about the mechanisms behind [brain](#) disorders, the authors said.

More information: Donna M. Werling et al, Whole-Genome and RNA Sequencing Reveal Variation and Transcriptomic Coordination in the Developing Human Prefrontal Cortex, *Cell Reports* (2020). [DOI: 10.1016/j.celrep.2020.03.053](https://doi.org/10.1016/j.celrep.2020.03.053)

Provided by Yale University

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