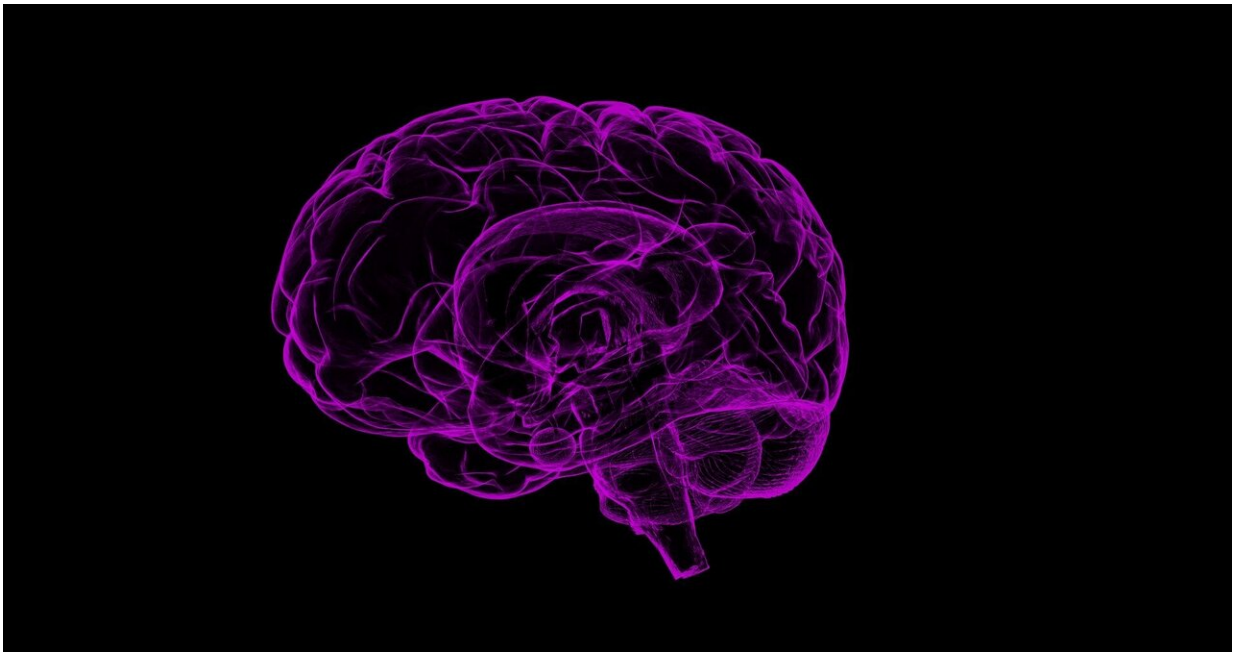
MedicalXpress

Genes expressed in the brain before birth may affect risk of childhood mental illness

May 18 2023



Credit: Pixabay/CC0 Public Domain

Researchers have identified various genes whose expression in the brain before birth may affect the risk of developing a range of mental illnesses during childhood. The team, which was led by investigators at Massachusetts General Hospital (MGH), a founding member of Mass General Brigham (MGB), published their findings recently in *Nature Neuroscience.*

Using data from the Adolescent Brain and Cognitive Development (ABCD) Study, a federally funded study of child and adolescent brain development that has enrolled nearly 12,000 individuals at age 9–10 years, the group first assessed whether genetic patterns that have been associated with psychiatric illnesses in adults also tracked with psychiatric symptoms in children.

"We found those relationships to be more complex than we had imagined. For example, genetic risk for ADHD and depression were associated with a range of symptoms in children, not just those related to attention or mood," says co–senior author Joshua Roffman, MD, director of MGH's Early Brain Development Initiative. "The genetic factors that shape mental illness symptoms in kids differ from the ones that shape mental illness symptoms in adults."

The strongest genetic predictor for most mental health symptoms in ABCD participants was a new measure, developed by co–senior author and computational geneticist Phil H. Lee, Ph.D., and colleagues at the Mass General Center for Genomic Medicine, that indexes risk not for a single disorder, but rather for a constellation of developmental disorders. The scientists refer to this new genetic measure as a "neurodevelopmental gene set," as it combines elements of genetic risk for several neurodevelopmental disorders, including autism, ADHD, Tourette syndrome, and depression.

Roffman, Lee, and their international collaborators found that this neurodevelopmental gene set also predicted childhood psychiatric symptoms in participants of the Generation R study, which included children of a similar age in the Netherlands.

Additional analyses of information from brain banks revealed that the genes in this set are expressed most strongly in the brain's cerebellum (which is most known for its involvement in complex motor functions),

and their expression in the cerebellum peaks before birth. Also, brain imaging data from the ABCD study indicated that children with psychiatric symptoms tended to have a slightly smaller cerebellum, perhaps a reflection of these genes' effects on cerebellar development during prenatal life.

"That genetic risk factors for mental illness in kids begin to influence the brain so early on—even before birth—means that interventions that protect them from risk may also need to start earlier in life than previously expected," says Roffman. "It is also important to note that while genes play an important part in risk for mental illness, the early life environment is also critical—and at this point, potentially easier to modify."

Indeed, certain prenatal exposures—such as folic acid—show promise for better brain health outcomes in children. "Our research team at Mass General is searching for other factors during pregnancy—whether in the realm of healthy lifestyle (such as quality sleep, exercise, and diet), optimal prenatal care, or psychosocial support—that can confer resiliency in developing brains and protect against risk of psychiatric disorders in young people."

One study, called Brain health Begins Before Birth (B4), is actively enrolling families at MGH during pregnancy and following brain development in children after birth.

More information: Joshua Roffman, Genetic patterning for child psychopathology is distinct from that for adults and implicates fetal cerebellar development, *Nature Neuroscience* (2023). DOI: 10.1038/s41593-023-01321-8.
www.nature.com/articles/s41593-023-01321-8

Provided by Massachusetts General Hospital