Low genetic risk for ADHD may protect against negative life experiences

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Credit: Nik Shuliahin, CC0

A recent study shows that people at low genetic risk for attention deficit hyperactivity disorder (ADHD) are not only less likely to have the disorder, they also have better than expected economic, health and behavioral outcomes in later life.

The results, published in the journal *Psychological Medicine*, "capture far more than just the risk and the absence of risk for a psychiatric

outcome," says study author James Li, a University of Wisconsin–Madison professor of psychology and investigator at the UW's Waisman Center. They suggest that individuals with low genetic risk for ADHD may be protected from many other negative life events that are seen in individuals with higher genetic risk.

For example, adults with lower genetic risk for ADHD also reported, on average, higher IQs and educational attainments, shorter or no criminal records, lower body mass index (BMI), and lower rates of depression than adults with middle-to-high genetic risk for ADHD.

Most psychiatric disorders are caused by lots of genes that each have a tiny influence on the disorder. Researchers can estimate a person's "genetic risk" for a psychiatric disorder by using their DNA to create something called a polygenic score (PGS), which adds up all the small genetic risk factors they carry. According to experts, the higher the number, the greater a person's genetic risk.

Li wondered whether the opposite was also true: Does a low PGS score always translate to a lower risk of disorder?

"Most researchers have just focused their attention on people with higher PGS," says Li. He became interested in people with lower PGS after an undergraduate student asked him in class what low risk factors for a condition tell us.

"I had no answer for that," Li says, despite teaching the subject extensively. "That day, I started running the analyses. And then I realized I had a paper on my hands that no one else has looked at."

The data for Li's paper came from a publicly available genome-wide association study (GWAS) for ADHD. This allowed him to look specifically at the genes for ADHD in a given individual and examine

how they relate to other outcomes that are typically associated with the disorder, such as level of education, depression, criminal records and BMI.

"GWAS identifies all the genetic variants that are statistically associated with ADHD, but with great statistical power," Li says.

ADHD is a good disorder to use as a litmus test for low PGS and its implications on other outcomes in life, he adds. ADHD is heritable and has a high prevalence in the U.S., where nearly 9 percent of children between the ages of six and 11 carry an ADHD diagnosis, and the disorder also exhibits predictable negative outcomes in adult life.

Li hopes his paper will encourage other researchers to further investigate the clinical implications of low PGS, especially in the context of other psychiatric disorders. He also plans to conduct a follow-up study to examine whether individuals with low PGS may also be more resistant to stressors in their lives.

He also appreciates that the idea for the paper came from a student.

"I think it helps me understand better how teaching really helps the science as much as the science helps the teaching," says Li. "My students are great scientists even if they don't know it. The questions they ask when there are no apparent answers are questions that can be answered through research methods."

More information: James J. Li. The positive end of the polygenic score distribution for ADHD: a low risk or a protective factor?, *Psychological Medicine* (2019). DOI: 10.1017/S0033291719003039

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