

## Genetic 'protection' against depression was no match for pandemic stress, finds study of first-year college students

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Living through a historic pandemic while handling the stress of the first year of college sent one-third of students in a new study into clinical



depression. That's double the percentage seen in previous years of the same study.

And while certain <u>genetic factors</u> appeared to shield first-year students in pre-pandemic years from <u>depression</u>, even students with these protective factors found themselves developing symptoms in the pandemic years.

In fact, much of the overall rise in <u>student</u> depression during the pandemic was among <u>young women</u> with this kind of "genetic resilience."

But the research has a silver lining.

By studying these students' experiences and backgrounds in depth and over time, scientists may have discovered a way to go beyond genetics to predict which students might be more or less vulnerable to stress-related depression.

The new study, "The impact of COVID-19 on a college freshman sample reveals genetic and nongenetic forms of susceptibility and resilience to stress," is published in the *Proceedings of the National Academy of Sciences* by a team from the Michigan Neuroscience Institute at the University of Michigan.

## Potential for prediction and prevention

The team used their findings to develop a tool called an Affect Score, that combines answers from a range of standard mental health questionnaires. The score could help colleges and universities offer more social and mental health support to those most at risk.

The score might work in other groups of people, too, alone or in



combination with genetic risk prediction for depression. But further research is needed.

The new findings come from a multi-year longitudinal effort to study the mental health, genetics, personal history, physical activity and sleep of successive groups of first-year college students. It began several years before the pandemic and continues today.

"These students' experiences during such a stressful time can help us understand the factors that contribute to a rise in depression risk, and inform future efforts to prevent it," said Huda Akil, Ph.D., senior author of the new paper and former co-director of the institute. "Understanding enough to predict is a key initial step to prevention, early detection and early treatment of depression."

Lead author Cortney Turner, Ph.D., an associate research scientist at MNI, says, "The possibility of preventing depression is what I'm most excited about, because the variables at baseline that appear to play the largest role in Affect Score may be modified with training." That might include summer programs before the start of freshman year to help students feel more confident and positive as they arrive on campus.

## Harnessing massive data

The team developed the Affect Score with the help of a machine learning tool that was used to comb through all the students' responses on thousands of standardized questionnaires and Fitbit data on their activity and sleep.

The data in the paper come from students in three cohorts of students, one that completed their freshman year before the pandemic, and two whose freshman experience was impacted by the pandemic.



At the start of their freshman year, all took 14 standard questionnaires and gave in-depth interviews conducted by Virginia Murphy-Weinberg, N.P., a highly experienced research nurse. They provided samples of blood and/or saliva to be analyzed in U-M's <u>Advanced Genomics Core</u>.

Samples were obtained on a wide range of biological measures prepandemic, but this became more limited for the two COVID-19 cohorts. Nevertheless, they contributed monthly salivary samples to measure stress and other hormones. Each student also received a Fitbit to monitor daily activity and sleep patterns.

The team also followed up with them multiple times with some of the same questionnaires during the rest of their freshman year and into the summer or next academic year to assess symptoms of depression and/or anxiety in each student.

By looking at which genetic variations each student carried on hundreds of thousands of genes, the researchers calculated their individual depression genetic risk score, called an MDD-PRS.

Men and women with a high MDD-PRS score were more likely than their classmates to develop depression as freshmen in the pre-pandemic era. But when the pandemic hit, genetics became less important.

Men with lower MDD-PRS scores were still less likely to develop depression during the pandemic, but not women with similarly low scores. Meanwhile, the overall risk for the group of students with high MDD-PRS scores didn't change much from the pre-pandemic classes.

The pandemic increased not only the incidence of depression in females, but how long it lasts, or its chronicity. No matter their genetic profile, women whose freshman year of college started in 2020 had over eight times the risk of chronic depression symptoms that lasted across that



first year and into the summer, compared with those who entered college before the year the pandemic hit, the study shows.

The study also identified what is termed "psychological resilience" in individuals whose genetic profiles might make them seem more prone to depression, but who didn't develop it despite going through all or part of their freshman year during a pandemic.

"This suggests that when the stress gets strong enough, genetic resilience alone is not enough to buffer against it, especially in females," said Akil. "But by using machine learning to analyze the components of the psychological profiles at baseline, our ability to predict who became depressed was truly remarkable."

She continued, "Both the genetic and nongenetic data tell us that nothing is predestined, and there are multiple kinds of resilience. Colleges and universities need to think about strategies for helping young people walk into their freshman year with the positive state of mind and social support that can help them weather stress, no matter what their background."

The team continues to test the Affect Score tool on freshmen who entered in 2021, 2022 and this fall. They're also preparing to test a validated psychiatric intervention digital tool that they hope will help with risk.

The students in the study were all from the University of Michigan, which offers mental health care and mental well-being support through its Counseling and Psychological Services and its University Health Service.

Akil and Turner are members of the U-M Eisenberg Family Depression Center, which offers multiple programs to support the mental health of



college students including athletes and veterans. For more than 20 years, the center has sponsored a national conference called Depression on College Campuses; the next conference will occur in March.

The center also offers a free online Depression Toolkit to support those experiencing depression symptoms and those who want to help them.

In addition to Akil, Turner and Murphy-Weinberg, the research team included Huzefa Khalil, Ph.D. and other MNI faculty, staff and trainees.

**More information:** Cortney A. Turner et al, The impact of COVID-19 on a college freshman sample reveals genetic and nongenetic forms of susceptibility and resilience to stress, *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2305779120

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