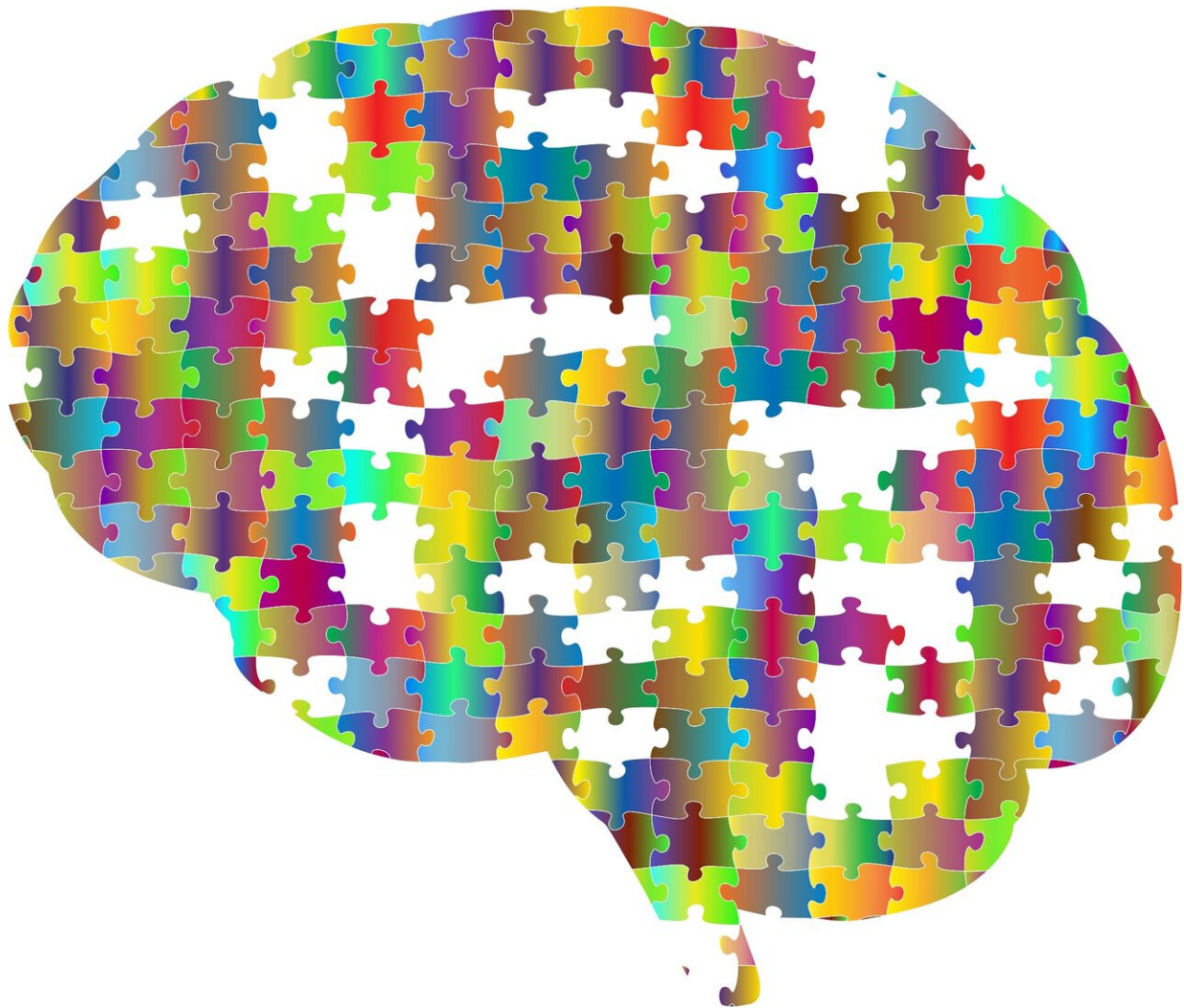


# Brain structure differences in teens may signal early substance use risk

December 30 2024

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[A study of nearly 10,000 adolescents](#) has identified distinct differences in the brain structures of those who used substances before age 15 compared to those who did not. Many of these structural brain differences appeared to exist in childhood before any substance use, suggesting they may play a role in the risk of substance use initiation later in life, in tandem with genetic, environmental, and other neurological factors.

"This adds to some emerging evidence that an individual's brain structure, alongside their unique genetics, environmental exposures, and interactions among these factors, may impact their level of risk and resilience for substance use and addiction," said Nora Volkow M.D., director of NIDA.

"Understanding the complex interplay between the factors that contribute and that protect against [drug use](#) is crucial for informing effective prevention interventions and providing support for those who may be most vulnerable."

Among the 3,460 adolescents who initiated substances before age 15, most (90.2%) reported trying alcohol, with considerable overlap with nicotine and/or cannabis use; 61.5% and 52.4% of kids initiating nicotine and cannabis, respectively, also reported initiating alcohol.

Substance initiation was associated with a variety of brain-wide (global) as well as more regional structural differences primarily involving the cortex, some of which were substance-specific. While these data could someday help inform clinical prevention strategies, the researchers emphasize that brain structure alone cannot predict substance use during adolescence, and that these data should not be used as a diagnostic tool.

The study, published in *JAMA Network Open*, used data from the Adolescent Brain Cognitive Development Study, (ABCD Study), the

largest longitudinal study of brain development and health in children and adolescents in the United States.

Using data from the ABCD Study, researchers from Washington University in St. Louis assessed MRI scans taken of 9,804 children across the U.S. when they were ages 9 to 11—at "baseline"—and followed the participants over three years to determine whether certain aspects of brain structure captured in the baseline MRIs were associated with early substance initiation.

They monitored for alcohol, nicotine, and/or cannabis use, the most common substances used in early adolescence, as well as use of other illicit substances. The researchers compared MRIs of 3,460 participants who reported substance initiation before age 15 from 2016 to 2021 to those who did not (6,344).

They assessed both global and [regional differences](#) in brain structure, looking at measures like volume, thickness, depth of brain folds, and surface area, primarily in the brain cortex.

The cortex is the outermost layer of the brain, tightly packed with neurons and responsible for many higher-level processes, including learning, sensation, memory, language, emotion, and decision-making. Specific characteristics and differences in these structures—measured by thickness, [surface area](#), and volume—have been linked to variability in cognitive abilities and neurological conditions.

The researchers identified five brain structural differences at the global level between those who reported substance initiation before the age of 15 and those who did not. These included greater total brain volume and greater subcortical volume in those who indicated substance initiation.

An additional 39 brain structure differences were found at the regional

level, with approximately 56% of the regional variation involving cortical thickness. Some brain structural differences also appeared unique to the type of substance used.

In a post-hoc analysis, the researchers found that many of these brain differences still held even after removing those participants who reported substance initiation prior to collection of their baseline MRIs.

The resulting comparison was between those who did not report any substance use initiation and a subgroup of 1,203 participants in the substance use initiation group who did not have any substance use experience when their MRIs were first captured.

The results of this secondary analysis suggest that some of these brain structural differences may exist prior to any substance use, challenging the interpretation that such differences are only driven by substance exposure and pointing to an area for further investigation.

While some of the brain regions where differences were identified have been linked to sensation-seeking and impulsivity, the researchers note that more work is needed to delineate how these structural differences may translate to differences in brain function or behaviors. They also emphasize that the interplay between genetics, environment, brain structure, the prenatal environment, and behavior influence, affect behaviors.

Another recent [analysis of data from the ABCD study](#) conducted by the University of Michigan demonstrates this interplay, showing that patterns of functional brain connectivity in early adolescence could predict substance use initiation in youth, and that these trajectories were likely influenced by exposure to pollution.

Future studies will be crucial to determine how initial brain structure

differences may change as children age and with continued substance use or development of substance use disorder.

"Through the ABCD study, we have a robust and large database of longitudinal data to go beyond previous neuroimaging research to understand the bidirectional relationship between [brain structure](#) and substance use," said Alex Miller, Ph.D., the study's corresponding author and an assistant professor of psychiatry at Indiana University.

"The hope is that these types of studies, in conjunction with other data on environmental exposures and genetic risk, could help change how we think about the development of substance use disorders and inform more accurate models of addiction moving forward."

**More information:** *JAMA Network Open* (2024). [DOI: 10.1001/jamanetworkopen.2024.52027](#)

Provided by National Institutes of Health

Citation: Brain structure differences in teens may signal early substance use risk (2024, December 30) retrieved 22 January 2025 from <https://medicalxpress.com/news/2024-12-brain-differences-teens-early-substance.html>

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