

Problems with 'pruning' brain connections linked to adolescent mental health disorders

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Problems with the brain's ability to "prune" itself of unnecessary

connections may underlie a wide range of mental health disorders that begin during adolescence, according to research published today.

The findings, from an international collaboration, led by researchers in the U.K., China and Germany, may help explain why people are often affected by more than one mental health disorder, and may in future help identify those at greatest risk.

One in seven adolescents (aged 10–19 years old) worldwide experiences mental health disorders, according to the World Health Organization (WHO). Depression, anxiety and behavioral disorders, such as attention deficit hyperactivity disorder (ADHD), are among the leading causes of illness and disability among young people, and adolescents will commonly have more than one [mental health disorder](#).

Many [mental health problems](#) emerge during adolescence. Among these are disorders such as depression and anxiety, which manifest as "internalizing" symptoms, including low mood and worrying. Other conditions such as [attention deficit hyperactivity disorder](#) (ADHD) manifest as "externalizing" symptoms, such as impulsive behavior.

Professor Barbara Sahakian from the Department of Psychiatry at the University of Cambridge said, "Young people often experience multiple mental health disorders, beginning in adolescence and continuing—and often transforming—into adult life. This suggests that there's a common brain mechanism that could explain the onset of these mental health disorders during this critical time of [brain development](#)."

In a study published today (April 24) in *Nature Medicine*, the researchers say they have identified a characteristic pattern of brain activity among these adolescents, which they have termed the "neuropsychopathological factor," or NP factor for short.

The team examined data from 1,750 adolescents, aged 14 years, from the IMAGEN cohort, a European research project examining how biological, psychological, and [environmental factors](#) during adolescence may influence brain development and mental health. In particular, they examined imaging data from brain scans taken while participants took part in cognitive tasks, looking for patterns of brain connectivity—in other words, how different regions of the brain communicate with each other.

Adolescents who experienced mental health problems—regardless of whether their disorder was one of internalizing or externalizing symptoms, or whether they experienced multiple disorders—showed similar patterns of brain activity. These patterns—the NP factor—were largely apparent in the frontal lobes, the area at the front of the brain responsible for executive function which, among other functions, controls flexible thinking, self-control and emotional behavior.

The researchers confirmed their findings by replicating them in 1,799 participants from the ABCD Study in the U.S., a long-term study of brain development and child health, and by studying patients who had received psychiatric diagnoses.

When the team looked at [genetic data](#) from the IMAGEN cohort, they found that the NP factor was strongest in individuals who carried a particular variant of the gene IGSF11 that has been previously associated with multiple mental health disorders. This gene is known to play an important role in synaptic pruning, a process whereby unnecessary brain connections—synapses—are discarded. Problems with pruning may particularly affect the frontal lobes, since these regions are the last brain areas to complete development in adolescents and young adults.

Dr. Tianye Jia from the Institute of Science and Technology for Brain-Inspired Intelligence, Fudan University, Shanghai, China and the

Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, U.K. said, "As we grow up, our brains make more and more connections. This is a normal part of our development. But too many connections risk making the brain inefficient. Synaptic pruning helps ensure that brain activity doesn't get drowned out in 'white noise.'

"Our research suggests that when this important pruning process is disrupted, it affects how brain regions talk to each other. As this impact is seen most in the frontal lobes, this then has implications for mental health."

The researchers say that the discovery of the NP factor could help identify those young people at greatest risk of compounding mental health problems.

Professor Jianfeng Feng from Fudan University in Shanghai, China, and the University of Warwick, U.K., said, "We know that many [mental health disorders](#) begin in adolescence and that individuals who develop one disorder are at increased risk of developing other disorders, too. By examining brain activity and looking for this NP factor, we might be able to detect those at greatest risk sooner, offering us more opportunity to intervene and reduce this risk."

More information: Tianye Jia, A shared neural basis underlying psychiatric comorbidity, *Nature Medicine* (2023). [DOI: 10.1038/s41591-023-02317-4](https://doi.org/10.1038/s41591-023-02317-4).
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