Wiring of the 'little brain' linked to multiple forms of mental illness

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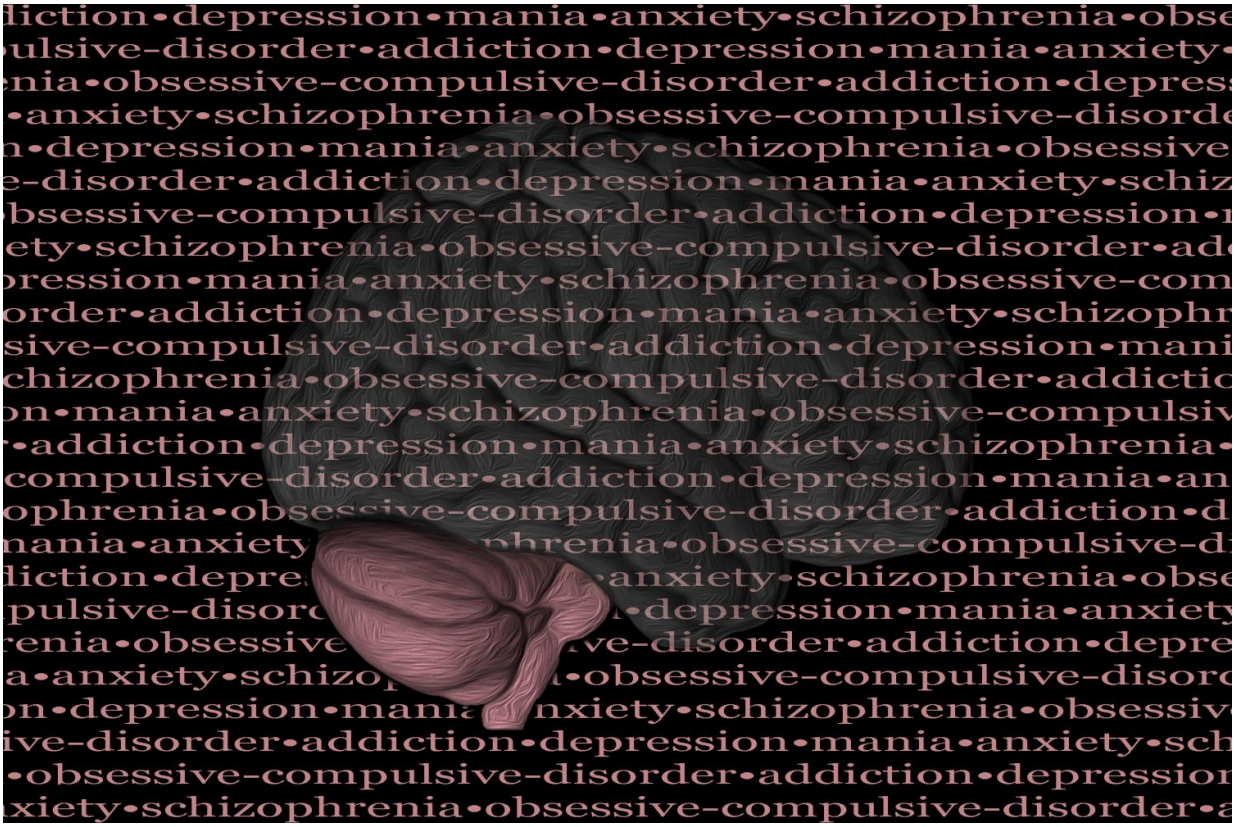

Duke researchers have linked specific differences in the brain's cerebellum (pink) and pons to increased risk for multiple forms of mental disorder. Credit: Annchen Knodt

A Duke University study is the first to link specific differences in brain

structure to what is common across many types of mental illness.

Having a single mental illness like anxiety, depression or schizophrenia is hard enough on its own. But studies consistently show that up to half of people with one mental illness also experience one or more additional forms of mental illness at the same time.

The high numbers of patients who suffer from multiple forms of mental illness has many researchers shifting focus away from studying individual disorders and instead hunting for common mechanisms or risk factors that might cause all types of mental disorders.

"The fact that comorbidity rates are so high is kind of mind-boggling," said Adrienne Romer, a clinical psychology graduate student in neuroscience and psychology at Duke University.

The findings, based on personal interviews and brain scans from over a thousand Duke undergraduates, show that individuals exhibiting symptoms that cross over many types of mental illness consistently exhibit differences in unexpected regions of the brain: the cerebellum, or "little brain," and the pons, structures that are traditionally known for helping us coordinate complex movements.

"Individuals with comorbidity tend to have worse outcomes in treatment, and that could be because we are not targeting the actual underlying process of what is shared among the disorders," Romer said. "We hope we could eventually use these findings to identify individuals at risk for developing multiple forms of mental disorder and determine the risk factors so that we can target those earlier on."

The study appeared April 11 in the journal *Molecular Psychiatry*.

Recent analyses of mental health data from a wide variety of

communities have shown that psychiatric symptoms tend to be highly correlated. That means, for example, a person who reports symptoms of anxiety is also more likely to report symptoms of other conditions like depression, bipolar disorder or obsessive-compulsive disorder.

Researchers have summarized these correlations in a score called the "p-factor."

"Higher p-factor scores indicate greater comorbidity across common forms of mental illness, and are associated with greater dysfunction, more severe illness and more hospitalizations," said Ahmad Hariri, a professor of psychology and neuroscience at Duke and senior author on the study.

But knowing that some people experience many types of mental health symptoms, on its own, does little to help doctors identify or treat at-risk patients. Romer and Hariri wanted to know if these p-factor scores could be linked to specific changes in the brain that might begin to shed light on what ultimately causes mental health disorders.

They drew on data from 1,246 Duke undergraduate students who participated in the Duke Neurogenetics Study. Participants in the study completed comprehensive mental health assessments and also underwent Magnetic Resonance Imaging (MRI). All participants who were diagnosed with mental disorders were referred for treatment.

Working with colleague and coauthor, Avshalom Caspi, also a professor of psychology and neuroscience at Duke, Romer first used information from the assessments to estimate each individual's p-factor score. She then used the MRI data to test correlations between the estimated p-factor scores and grey matter volume, a measure of brain density, and the "integrity" of white matter pathways throughout the brain.

She and the team were surprised to find that higher p-factor scores were correlated with lower grey matter volume in the cerebellum, a region of the brain that has traditionally been associated more with motor function and coordination than with emotion and thinking.

She also found that students with higher p-factor scores showed less integrity of white matter pathways within the pons, which includes wiring that connects the cerebellum with higher-order reasoning centers in the prefrontal cortex. These connections are known to play a key role in providing feedback on how well our movements are in sync with our internal model of what we hope to achieve, so that we can update and change course accordingly.

These white matter pathways may also play a similar role in providing real-world feedback that helps us better regulate our thoughts and emotions, the researchers say.

"This work suggests that the p-factor may very well be tapping into inadequacies or deficiencies in simply our ability to monitor information—including our own thoughts and emotions—and make sure they jive with our intentions, our expectations and the responses that we get from the world outside," Hariri said. "When that goes awry, and the extent to which that goes awry, may result in either milder forms of mental illness or more and more severe forms of mental illness."

"There is growing reason to believe that variations in some brain networks predispose people to have any mental health problem, in a nonspecific way," said Benjamin Lahey, professor of epidemiology, psychiatry, and behavioral neuroscience at the University of Chicago, who was not involved in the study. "If these findings are replicated, they will be of great importance to how we understand the neural bases of psychological problems."

However, Lahey warns, it may be challenging to replicate the findings on a more diverse group than Duke undergraduates, who on the whole may be healthier and have higher intelligence scores than the general population.

The team plans to repeat the study in different populations, starting with New Zealanders participating in the long-term Dunedin study, and will seek more detailed MRI scans of the cerebellum in order to explore precisely what role this brain region plays in mental health.

"Outside of a pocket of dedicated researchers, the cerebellum is a largely neglected structure in neuropsychiatric research," Hariri said. "Cerebellum literally means 'little brain,' and we aim to give it a little more respect."

More information: A L Romer et al, Structural alterations within cerebellar circuitry are associated with general liability for common mental disorders, *Molecular Psychiatry* (2017). DOI: 10.1038/mp.2017.57

Provided by Duke University