Biomarker could help diagnosis schizophrenia at an early age
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Functional magnetic resonance imaging (fMRI) and other brain imaging technologies allow for the study of differences in brain activity in people diagnosed with schizophrenia. The image shows two levels of the brain, with areas that were more active in healthy controls than in schizophrenia patients shown in orange, during an fMRI study of working memory. Credit: Kim J, Matthews NL, Park S./PLoS One.

Scientists at Sanford Burnham Prebys have discovered how levels of a protein could be used in the future as a blood-based diagnostic aid for schizophrenia. The activity of the protein, which is found in both the brain and blood, affects neural connections in human brains and is uniquely imbalanced in people diagnosed with the condition. The research also provides guidance for future analyses into the molecular basis of this serious, disabling mental disorder.

The study, an international collaboration among groups at Yokohama City University Graduate School of Medicine in Japan and the Department of Psychiatry at Harvard Medical School in Belmont, Massachusetts, was recently published in PNAS.

"This study examined the activity of CRMP2, a protein found in the brain (called a 'cytoskeletal protein') that regulates how neurons make connections with each other," says Evan Y. Snyder, M.D., Ph.D., director of the Center for Stem Cells and Regenerative Medicine at Sanford Burnham Prebys and co-senior author of the study. "CRMP2 also happens to be expressed in lymphocytes in the blood and can therefore be readily sampled in people by doing nothing more than a simple venipuncture.

"There was an abundance of CRMP2 levels in samples from people with schizophrenia compared to people without the disorder. We also saw structural abnormalities in the dendrites of neurons that could potentially be disabling because dendrites play an important role in receiving impulses from other nerve cells in the brain."

Previous research has shown that most people maintain an even balance between the two forms of CRMP2: its active, non-phosphorylated form and its inactive, phosphorylated form. The new research first examined postmortem brain tissue and then blood samples from people with schizophrenia. The research team compared these levels to those in people without the disorder.

The findings indicated that the amount of active CRMP2 was too high in people with schizophrenia and, at least in young people with schizophrenia, was not balanced by an appropriate amount of increased inactive CRMP2. That imbalance between active and inactive CRMP2 could account for some dysfunctions in neural connections.

Measuring an abundance of active CRMP2, particularly if its ratio with inactive CRMP2 is too low, could become a format for a rapid, minimally invasive blood test to support the diagnosis of schizophrenia.

"Schizophrenia can be challenging to diagnose early on or in young patients for a number of reasons," says Snyder. "Pairing a blood test with
psychiatric and neurobehavioral exams could help doctors distinguish schizophrenia from other conditions that have somewhat similar symptomologies, such as the manic phase of bipolar disorder or other behavioral, personality, or thought disorders.

"Our results were most striking in people under the age of 40, and even more so in people under the age of 30. An early diagnosis could improve the clinical management of affected individuals as well as accelerate the development of new therapeutic options," Snyder adds.

The researchers now want to dig deeper into the molecular biology of the disease to discover the "regulator" that keeps most people's CRMP2 levels on an even keel. They also want to conduct a larger, multi-center clinical study that compares schizophrenia with other psychiatric disorders. Future research will aim to include a wider range of ethnicities and age groups.

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