

# Scientists zeroing in on psychosis risk factors

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The onset of schizophrenia and other psychotic disorders typically occurs at about 21 years of age, with warning signs beginning around age 17, on average. Credit: iStockphoto

During the first phase of a major national study, scientists have uncovered a new cluster of preclinical symptoms linked to a significant increase in the risk that a young person will go on to develop a psychotic illness, including schizophrenia. The consortium of researchers, from Emory and seven other universities, has also discovered several biological processes tied to the transition from subtle symptoms to clinical psychosis.

The onset of schizophrenia and other [psychotic disorders](#) typically occurs at about 21 years of age, with warning signs, known as a prodromal syndrome, beginning around age 17, on average. About 30 to 40 percent of youth who meet current criteria for a prodromal syndrome will develop schizophrenia or another psychotic disorder.

"We are moving at an unprecedented pace towards identifying more precise predictors," says Elaine Walker, an Emory professor of psychology

and neuroscience. "By increasing our understanding of the factors that give rise to [psychosis](#), we hope to ultimately improve the ability to provide preventive intervention."

Walker is one of the principal investigators in the [North American Prodrome Longitudinal Study](#) (NAPLS). The National Institute of Mental Health (NIMH) funded the ongoing study, which unites the efforts of Emory, the University of North Carolina, Yale, Harvard, the University of Calgary, UCLA and UC San Diego, and the Feinstein Institute at Hillside Hospital.

"The only way we can do this research is by having a large consortium, combining a range of expertise, from genetics to neuro-endocrinology, psychology and psychiatry," Walker says. "It is also difficult to identify individuals who are at risk for psychosis and in order to have enough statistical power, we need a large sample of study subjects."

The consortium has published a flurry of 60 papers during the past four years, involving more than 800 adolescents and young adults who were showing clinical warning signs of impending psychosis and a group of 200 healthy youth.

Among the key findings: Prodromal youth with elevated levels of the [stress hormone cortisol](#) and indicators of neuro-inflammation are more likely to become psychotic within a year.

"We've developed a risk-prediction algorithm, including measures of symptoms as well as biomarkers, that we have made available for clinicians," Walker says. "In the future, they can take saliva samples from at-risk patients to check cortisol levels, and to monitor those levels over time. As we get more information, we keep adding to the algorithm to improve the sensitivity and specificity of prediction. It's important because anti-psychotic medications have a lot of side effects. You don't want to give them to young people unless

you are fairly confident that they are on the way to a psychotic disorder." with schizophrenia are unable to hold a job or live independently for most of their lives. Preventing the onset of [schizophrenia](#) and other psychoses has become a major area of emphasis at the NIMH.

The researchers are now working on refining a blood-biomarker algorithm that clinicians could use to monitor at-risk patients for signs of neuro-inflammation, oxidative stress, hormones and metabolism.

In addition to medication, cognitive therapy and other interventions that reduce stress may be used to help an individual safely make it through the high-risk period, Walker says. "We've found that youth with the highest risk tend to be both exposed to more stress and more reactive to stress."

"Psychosis is extremely complex, there is no doubt about it, and we're learning that it's even more complex than we previously realized," Walker says. "But if we're ever going to make progress in prevention and treatment, we're going to have to come to grips with that complexity and fully understand it."

Provided by Emory University

The consortium of researchers also discovered that the brains of at-risk patients who later develop psychosis show a dramatic decline of gray matter in the year leading up to the diagnosis. And they found that the elevation in a patient's cortisol level predicts the magnitude of the decline in brain volume.

In 2008, the NIMH awarded \$25 million to the consortium for the first phase of the NAPLS project, which lasted five years.

The NAPLS project is now entering its second five-year phase through additional NIMH funding, including a \$2.4 million award to Emory.

"We have better technology than ever before for studying the human brain and changes in the brain over time," Walker says. "We're at an especially fruitful time in terms of discoveries we can make."

During phase two, "we will be looking more closely at hormones, especially stress hormones and indicators of neuro-inflammatory processes," Walker says. "And we're going to be looking much more closely at changes in brain structure and function over time. We're hoping to identify in real-time, with much greater clarity, what is causing what. In other words, the chain of neural mechanisms."

Schizophrenia, the most extreme psychosis, affects about 1 percent of the population and can have devastating consequences. Most people diagnosed

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