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Neurocognitive deficits may be a red flag for psychosis

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While schizophrenia is best known for episodes of psychosis - a break with reality during which an individual may experience delusions and hallucinations - it is also marked by chronic neurocognitive deficits, such as problems with memory and attention. A multi-site cognition study led by psychologists at Beth Israel Deaconess Medical Center (BIDMC) found that these neurocognitive symptoms are evident prior to the onset of psychosis in a high-risk stage of the disorder called the prodromal phase. Published today online in advance of print in *JAMA Psychiatry*, the findings suggest that these impairments may serve as early warning signs of schizophrenia, as well as potential targets for intervention that could mitigate the onset of the psychotic disorder and significantly improve cognitive function.

"To our knowledge, this is the largest and most definitive study of cognition in the high-risk period before onset of for psychosis/schizophrenia," said corresponding author Larry J. Seidman, PhD, a psychologist at BIDMC and professor of psychology at Harvard Medical School. "This is part of a paradigm shift in the way we are focusing on the earlier, prodromal phase of the disorder in an effort to identify those most likely to develop psychosis."

Seidman and colleagues collected neurocognitive functioning data from participants at eight university-based, outpatient programs in the United States and Canada over the course of four years. The observational study compared 689 males and females deemed at clinical high risk (CHR) of developing psychosis to 264 male and female healthy controls (HC).

Using 19 standard tests of executive and visuospatial abilities, attention and working memory, verbal abilities and declarative memory, the researchers found that the high-risk group performed significantly worse than the control group on all 19 measures. Among the high-risk individuals only, those who later progressed to a psychotic disorder performed significantly worse than their high-risk peers who did not develop psychosis during the study.

"Currently, when mental health professionals assess people coming in for evaluation, we don't know who will eventually develop schizophrenia," said Seidman. "Our group's focus is on identifying early warning signs and then developing interventions to improve a person's chances for not getting it, making it milder or delaying it."

Impaired working memory (the ability to hold information like a phone number in mind for a short time while it's in use) and declarative memory (the ability to recall things learned in the last few minutes) turned out to be the key neurocognitive functions that are impaired in the high-risk, prodromal phase prior to the onset of full-blown psychosis. These findings, said Seidman, are in keeping with the experiences of many people with schizophrenia who report sudden difficulties reading, concentrating or remembering things in the earliest days of the disorder.

Schizophrenia "conjures up dread" in our culture, Seidman said, but he notes that it is likely these cognitive deficits - not the delusions and hallucinations people fear so much - that keep roughly 80 percent of people with schizophrenia out of work or school. Recent focus on the prodromal period and the growing promise of early intervention is giving patients and their families more realistic hope that better outcomes are possible, he added.

"People can hear voices and still function pretty well, but they basically cannot function at all when their cognition is impaired," he said. "We are

also testing a number of cognitive remediation and enhancement treatments to determine their role in the evolution of the illness. There's more evidence suggesting that early intervention reduces the number of people who transition to schizophrenia."

This study represented the second phase of the North American Prodrome Longitudinal Study (NAPLS), the multi-site research consortium formed in 2003 to focus on early intervention and prevention of schizophrenia. By pooling their data, NAPLS researchers have been able to identify individuals at high risk for developing a psychotic disorder as well as the biological risk factors associated with converting to psychosis. This summer, the collaborators, led by researchers at Yale, published a risk calculator that can help professionals predict patients' risk of developing psychosis. In addition to BIDMC and Yale, the other NAPLS sites are based at Emory University, the University of Calgary, University of California Los Angeles (UCLA), University of California San Diego (UCSD), University of North Carolina Chapel Hill, University of San Francisco, and Zucker Hillside Hospital.

"A significant number of people are able to remain in or go back to work and school," Seidman said. "This early intervention approach is giving people more hope, and that really matters."

Provided by Beth Israel Deaconess Medical Center