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Alterations in brain's white matter key to schizophrenia, study shows

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Schizophrenia, a chronic and debilitating disorder marked in part by auditory hallucinations and paranoia, can strike in late adolescence or early adulthood at a time when people are ready to stand on their own two feet as fully independent adults.

Now scientists at UCLA think they are beginning to understand one important piece of this puzzle. In the first study of its kind, the researchers used a novel form of brain imaging to discover that white matter in the brains of adolescents at risk of developing schizophrenia does not develop at the same rate as healthy people. Further, the extent of these alterations can be used to predict how badly patients will or will not deteriorate functionally over time.

Reporting in the online edition of the journal *Biological Psychiatry*, lead author Katherine Karlsgodt, a postdoctoral fellow in UCLA's Department of Psychology, and senior authors Tyrone Cannon and Carrie Bearden, professors at the UCLA Semel Institute for Neuroscience and Human Behavior, focused on the brain's white matter — which forms the major connections between different brain regions — because it is known that white matter is disrupted in people who already have schizophrenia.

"We found that healthy subjects showed a normal and expected increase in measures indexing white matter integrity in the temporal lobe as they age," said Karlsgodt, "but young people at high-risk for psychosis showed no such increase — that is, they fail to show the normal

developmental pattern."

While there is growing evidence that schizophrenics show changes in white matter, and there is increasing evidence that white matter connectivity may be highly relevant to the development of psychosis, there is very little known about how these changes arise, said Karlsgodt. Historically, looking at white matter has been hard to do. But in recent years, she said, researchers have
begun to use a relatively new technique, diffusion tensor imaging (DTI) that uses the movement of water molecules along white matter tracts to map out the brain's pathways. In the last few years, these techniques have been applied to research schizophrenia and other disorders.

The researchers studied a control group of 25 healthy individuals and 36 teens and young adults, aged 12 to 26, at very high risk for developing schizophrenia, and followed them over a two-year period. The adolescents were identified as high risk due to genetic factors (i.e., being close relatives of someone with schizophrenia), or because they showed very early clinical symptoms of the disease. All of the subjects underwent a DTI scan at the start of the trial, along with clinical and functional assessments. Follow-up assessments of clinical and functional outcome were done at different periods over the next two years.

Failing to find a normal increase in white matter integrity over time in the at-risk subjects, said Karlsgodt, "suggests there is a fundamental difference in how typically developing young people and high-risk adolescents develop during this period right before the disease would be expected to manifest. Something may go awry with the developmental process during this period that might contribute to the onset of the disorder."

The other important finding, she said, was that by looking at white matter integrity in the temporal lobe at people's first appointment, "we

could predict how well they would be functioning 15 months later at work, school and home.

"This is a very exciting finding, because it means we might be closer to being able to identify people who will need more or different treatments in the future, so that we can get them the help they need."

Source: University of California - Los Angeles