

Siblings of schizophrenia patients display subtle shape abnormalities in brain

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Subtle malformations in the brains of patients with schizophrenia also tend to occur in their healthy siblings, according to investigators at the Silvio Conte Center for the Neuroscience of Mental Disorders at Washington University School of Medicine in St. Louis. Shape abnormalities were found in the brain's thalamus.

The researchers performed brain MRI scans in 25 patients with schizophrenia and their non-affected siblings and compared the scans with those of 40 healthy volunteers and their siblings. Comparisons were possible through a process that converts images into three-dimensional models of brain anatomy, called high-dimensional brain mapping. The technique allows scientists to detect tiny differences in brain anatomy.

"We're interested in the thalamus because it has a lot of connections to the prefrontal cortex," says Michael P. Harms, Ph.D., senior scientist at the Conte Center. "In addition to psychosis, schizophrenia is characterized by other difficulties, such as issues with working memory and decreased cognitive performance. Those symptoms are believed to involve the cortex, and since the thalamus projects throughout the cortex, it's conceivable abnormalities in the thalamus may be related to those symptoms."

Since individuals with schizophrenia and their healthy siblings showed evidence of the same shape abnormalities in the thalamus, the researchers want to look more closely to determine whether these deformations may represent biological markers of disease risk.

"We devised a mathematical approach and developed a shape score based on the differences in shape that we observed between those with schizophrenia and the healthy control subjects," Harms explains. "Then we computed shape scores for the siblings of the schizophrenia patients. Their scores landed between the scores of the controls

and the individuals with schizophrenia. The siblings had an intermediate degree of deformation in the thalamus."

The thalamus relays information from every sensory system but smell to the cortex, and it connects to diverse structures throughout the brain. The walnut-sized thalamus is made up of several distinct sub-regions, and the researchers found that compared to control subjects, the front and back ends of the thalamus were deformed inward in those with schizophrenia. The same deformations were present, but less pronounced, in the siblings of schizophrenia patients.

About 1 percent of the general population suffers from schizophrenia. Even after the initial symptoms of psychosis are treated with medication and psychotherapy, patients can relapse. And with each relapse, the patient's condition can get worse. Even the best possible outcome — no future relapses of psychotic symptoms — still requires patients to take antipsychotic medications for the rest of their lives.

"Early diagnosis and intervention with the most effective antipsychotic medications and psychotherapies may offer the best hope for patients with schizophrenia and their families," says co-investigator John G. Csernansky, M.D., the Gregory B. Couch Professor of Psychiatry and Neurobiology at the School of Medicine and director of the Conte Center. "This type of brain-structure analysis eventually may make it possible to start treatment for schizophrenia more quickly, perhaps even before full-blown psychotic symptoms, such as hallucinations and delusions, occur."

Harms and Csernansky say it's possible that shape changes in the thalamus may represent a biological marker for schizophrenia, called an endophenotype, but they can't be sure until these structural changes can be linked to the symptoms of the illness. Some of those studies are underway

now. The current study was published in the Dec. 12 issue of *The Journal of Neuroscience*.

Source: Washington University

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