Brain-scan abnormalities found in children with pediatric acute-onset neuropsychiatric syndrome

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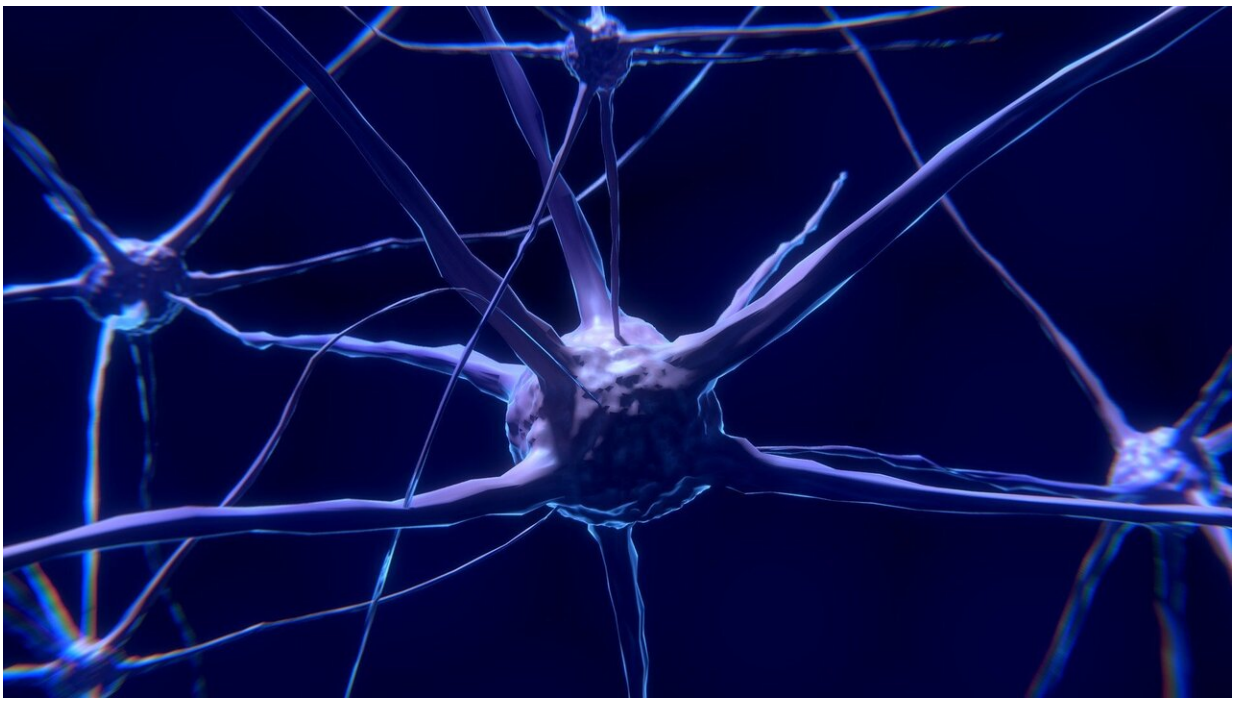

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Subtle abnormalities occur in key brain structures of children diagnosed with pediatric acute-onset neuropsychiatric syndrome, a disease characterized by abrupt, severe behavioral problems, according to a new study from the School of Medicine.

The findings, reported in a paper published May 4 in *JAMA Network Open*, may help resolve an ongoing debate about whether these symptoms represent a disease, which is also referred to by its acronym, PANS.

The disorder is characterized by sudden onset of extreme obsessive-compulsive symptoms; food-related fears that can cause the patient to stop eating; cognitive problems, such as loss of reading ability and math skills; and severe behavioral regression. Many cases of PANS occur after an acute infection, and the disorder is thought to result from an immune-system attack on the brain. Yet some clinicians attribute the symptoms to psychosocial factors.

"It's a very dramatic, severe and disruptive illness," said the study's co-lead author, Jennifer Frankovich, MD, clinical associate professor of pediatrics at Stanford and a pediatric rheumatologist at the Stanford Children's Health Immune Behavioral Health Clinic, where she cares for children with PANS and directs the Stanford PANS Research Program.

Many families struggle to obtain appropriate care for these children. "The biggest problem these families face is that most clinicians don't think this is a real illness," Frankovich said. "When you see a child that's completely out of control, it's easy to say, "This is a dysfunctional family; that's the cause of the child's illness." But if it was family dynamics causing the child's psychiatric symptoms, I don't think you would see this brain finding."

Comparing MRI scans

The study analyzed MRI scans of the brains of 34 children with PANS, as well as those of 64 children in a control group. Children in the control group had received MRIs as part of their medical care but did not have symptoms of PANS.

The PANS and control brain scans did not show differences visible to the naked eye, such as large lesions. However, analyzing the scans with software that detects microstructural differences revealed abnormalities in certain brain regions in children with PANS. The software compared all regions of the brain in the two groups of scans without prejudice toward any specific area. The regions that showed abnormalities in children with PANS matched those predicted to be abnormal on the basis of their behavioral problems.

Children with PANS had greater water diffusivity, meaning more movement of water molecules, in specific brain structures in the deep gray matter, including the thalamus, basal ganglia and amygdala. The thalamus helps relay nerve signals from the spinal cord and base of the brain to the gray matter. The basal ganglia help control motor and eye movements, learning procedures and habits, cognition, and emotion. The amygdala is the brain's fear center.

"It was interesting that we were able to identify microstructure alterations in these patients in regions hypothesized to be abnormal based on their clinical symptoms," said the study's senior author, Kristen Yeom, MD, associate professor of radiology. Greater water diffusivity in these regions suggests inflammation or swelling, or possibly another type of structural alteration in the brain, she said, adding that more research will be needed to determine the meaning of the findings.

About half of the children with PANS had subtle neurological problems that could be detected on a physical exam, and these problems included indicators of basal ganglia dysfunction, Frankovich noted. Even the children with PANS who did not have these abnormal physical exam findings still had differences on their brain MRIs, the study found. "If they did have these subtle findings on a neurological exam, their brain MRI had more extensive microstructural changes," Frankovich said.

More research is needed to explore questions such as whether the brain changes differ with new-onset versus chronic PANS, and whether treatment for PANS might reverse the brain abnormalities, the scientists said.

"We would love to get funding to study these kids' brains in remission," Frankovich said. "We don't know yet whether or not their brains go back to normal after an episode. I think this is really important to understand."

More information: Jimmy Zheng et al. Association of Pediatric Acute-Onset Neuropsychiatric Syndrome With Microstructural Differences in Brain Regions Detected via Diffusion-Weighted Magnetic Resonance Imaging, *JAMA Network Open* (2020). DOI: 10.1001/jamanetworkopen.2020.4063

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