Imaging study demonstrates how the 'social brain' is functionally impaired in autism

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A team of UCLA scientists has found that brain areas linked to social behaviors are both underdeveloped and insufficiently networked in youths with high functioning autism spectrum disorder (ASD) compared to study participants without ASD.

The findings, which appear in the online issue of the peer-reviewed journal *Brain and Behavior*, provide insight into how the brains of children and adolescents with ASD might be organized differently than youths without the disorder, says study first author Kay Jann, a postdoctoral researcher in the UCLA Department of Neurology.

The study advances the basic understanding of the ASD brain, Jann said.

"The brain controls most of our behavior and changes in how brain areas work and communicate with each other can alter this behavior and lead to impairments associated with mental disorders," he said. "When you match physiologic changes in the brain with behavioral impairment, you can start to understand the biological mechanisms of this disorder, which may help improve diagnosis, and, in time, treatment."

The researchers used imaging technology that tracks both brain blood flow—as a measure of energy use—and the organization and strength of connections within intrinsic neural networks.

This was the first time an MRI tool known as arterial spin labeling perfusion was used to study ASD. The technique uses magnetically labeled blood water as a tracer to quantify brain blood flow. The researchers also refined use of existing technology that assesses how well separate brain areas are functionally interconnected. Both techniques are non-invasive, requiring no injections of radioactive tracers.

This approach has been used in other brain disorders, such as schizophrenia, which has already led to novel insights and alternative treatment approaches in that disorder.

"In neurocognitive or neuropsychiatric disorders, these two crucial properties—functional organization of the brain and its accompanying energy demands—are often found to be altered," said study senior author Danny J.J. Wang, an associate professor of neurology at UCLA.

In this study, investigators studied 17 youths with high-functioning ASD and 22 typically developing children and adolescents. The groups were matched by age, 7 to 17 years old, gender and IQ scores.

The hypothesis researchers were testing is that ASD might be caused by increased or decreasedconnectivity within specific neural networks that form the "social brain." This connectivity can be measured by the amount of blood flow and activity patterns between brain nodes, or neural networks.

"One major brain network, the default mode network, has become a focus of such research, because it is important for social and emotional processes, self-referential thought, and in 'Theory of Mind,' which is the ability to attribute mental states to one-self and to others," Wang said. "These are cognitive processes that are to some extent impaired in persons with autism spectrum disorders."

Imaging the participants while they rested in the scanners revealed significant differences between the two groups, Wang said. Children with ASD exhibited a pattern of widespread increased blood flow, or hyper-perfusion, linked to increased oxygen metabolism in frontal brain areas that are important in navigating social interactions.

This is important because, as a brain develops,

blood flow is generally reduced. These signs of continuing hyper-perfusion in ASD participants suggest delayed neurodevelopment in these frontal brain regions associated with socio-emotional cognition, Wang said.

Researchers say this is consistent with structural MRI findings of enlarged brain size and an overabundance of neurons in ASD, due to the fact that the synapses of neurons have not been sufficiently "pruned" as the brain develops. Too many functioning synapses inhibit cognition while requiring extra blood flow.

The research team also discovered reduced long-range connectivity between default mode network nodes located in the front and back of the brain in those with ASD, compared to typical brains. This loss of connectivity means that information cannot flow as it should between distant areas of the brain, which may help explain impairment in social responsiveness, Jann said.

"The architecture of the brain follows a cost efficient wiring pattern that maximizes functionality with minimal energy consumption," Jann said. "This is not what we found in our ASD participants."

Going forward, the team will continue to study the relationship between network connectivity and metabolism in individuals with ASD, extending their work to other relevant brain networks. They're also seeking to define the range of variation in these factors in the general population.

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