Autism Linked with Excess of Neurons in Prefrontal Cortex

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A study by researchers at the University of California, San Diego Autism Center of Excellence shows that brain overgrowth in boys with autism involves an abnormal, excess number of neurons in areas of the brain associated with social, communication and cognitive development.

The scientists discovered a 67 percent excess of cortical cells – a type of brain cell only made before birth – in children with autism. The findings suggest that the disorder may arise from prenatal processes gone awry, according to lead researcher Eric Courchesne, PhD, professor of neurosciences at the UC San Diego School of Medicine and director of the Autism Center of Excellence.

Click on the photo to watch video of Dr. Courchesne discussing this research.

Relying on meticulous, direct cell counting, the study – to be published November 9 by the *Journal of the American Medical Society* (*JAMA*) and funded in part by the National Institutes of Health – confirms a relatively recent theory about possible causes of autism.

Small head circumference at birth, followed by a sudden and excessive increase in head circumference during the first year of life, was first linked to development of autism by Courchesne's team in 2003, in a paper published in *JAMA*.

In the new study, Courchesne and colleagues compared postmortem tissue from the prefrontal cortex of seven boys, ages 2 to 16 years, who had autism, to that of six typically developing boys. The prefrontal cortex is part of the brain's outermost cortical layer, comprising roughly one-third of all cortical gray matter. It is the part of the brain involved in social, language, communication, affective and cognitive functions – functions most disrupted in autism.

"Brain imaging studies of young children with autism have shown overgrowth and dysfunction in the prefrontal cortex as well as other brain regions," said Courchesne. "But the underlying cause at the level of brain cells has remained a mystery. The best guess was that overgrowth of prefrontal cortex might be due to an abnormal excess of brain cells, but this had never been tested."

Using an advanced computerized analysis system developed by co-investigator Peter Mouton, PhD, of the University of South Florida, along with blinded anatomical and cell count measurements, the study found that children with autism had 67 percent more neurons in the prefrontal cortex than control subjects. The brains of the autistic children also weighed more than those of typically developing children of the same age.

"Because new cortical neurons are not generated after birth, the increase in neuron numbers in children with autism points to prenatal processes," said Courchesne. He went on to explain that proliferation of such neurons is exponential between 10 and 20 weeks gestation and normally results in an overabundance of neurons at this point in fetal development. However, during the third trimester of pregnancy and early life of an infant, about half of those neurons are normally removed in a process called apoptosis (cell death). A failure of that key early developmental process would create a large pathological excess of cortical neurons.

"An excess of brain cells was found in each child with autism that we studied," said Courchesne. "While we think that ultimately not every child with an autism disorder will show this, our study does suggest that an abnormal excess of cells may be quite common among children with autism. This is an exciting finding because, if future research can pinpoint why an excessive number of brain cells are there in the first place, it will have a large impact on understanding autism, and perhaps developing new treatments."

Potential avenues for future study include the molecular and genetic mechanisms involved in regulating early neuron production or in managing normal cell attrition that occurs late in pregnancy and during early life.

Additional contributors to the study include Peter R. Mouton, PhD, University of South Florida School of Medicine Alzheimer's Institute and Research Institute; Michael E. Calhoun, PhD, Sinq Systems, Silver Spring, MD; Katerina Semendeferi, PhD, UC San Diego Department of Anthropology; and Cielia Ahrens-Barbeau; Melodies J. Hallet, Cynthia Carter Barnes, PhD, and Karen Pierce, PhD, UCSD Department of Neurosciences and Autism Center of Excellence.

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Media Contact: Debra Kain, 619-543-6163, ddkain@ucsd.edu