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Study shows gene defect's role in autism-like behavior

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Scientists affiliated with the UC Davis MIND Institute have discovered how a defective gene causes brain changes that lead to the atypical social behavior characteristic of autism. The research offers a potential target for drugs to treat the condition.

Earlier research already has shown that the gene is defective in children with autism, but its effect on neurons in the brain was not known. The new studies in mice show that abnormal action of just this one gene disrupted energy use in neurons. The harmful changes were coupled with antisocial and prolonged repetitive behavior -- traits found in autism.

The research is published online today in the scientific journal *PLoS ONE*.

"A number of genes and environmental factors have been shown to be involved in autism, but this study points to a mechanism -- how one gene defect may trigger this type of neurological behavior," said study senior author Cecilia Giulivi, professor of molecular biosciences in the UC Davis School of Veterinary Medicine and a researcher affiliated with the UC Davis MIND Institute.

"Once you understand the mechanism, that opens the way for developing drugs to treat the condition," she said.

The defective gene appears to disrupt neurons' use of energy, Giulivi said, the critical process that relies on the cell's molecular energy

factories called mitochondria.

In the research, a gene called pten was tweaked in the mice so that neurons lacked the normal amount of pten's protein. The scientists detected malfunctioning mitochondria in the mice as early as 4 to 6 weeks after birth.

By 20 to 29 weeks, DNA damage in the mitochondria and disruption of their function had increased dramatically. At this time the mice began to avoid contact with their litter mates and engage in repetitive grooming behavior. Mice without the single gene change exhibited neither the mitochondria malfunctions nor the behavioral problems.

The antisocial behavior was most pronounced in the mice at an age comparable in humans to the early teenage years, when schizophrenia and other behavioral disorders become most apparent, Giulivi said.

The research showed that, when defective, pten's protein interacts with the protein of a second gene known as p53 to dampen energy production in neurons. This severe stress leads to a spike in harmful mitochondrial DNA changes and abnormal levels of energy production in the cerebellum and hippocampus -- brain regions critical for social behavior and cognition.

Pten mutations previously have been linked to Alzheimer's disease as well as a spectrum of autism disorders. The new research shows that when pten protein was insufficient, its interaction with p53 triggered deficiencies and defects in other proteins that also have been found in patients with learning disabilities including autism.

Provided by UC Davis