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Brain scientists spot nature/nurture gene link

July 16 2008

(PhysOrg.com) -- Neuroscientists at MIT's Picower Institute for Learning and Memory found that a previously unsuspected set of genes links nature and nurture during a crucial period of brain development.

The results, reported in the July 8 issue of the *Proceedings of the National Academy of Sciences (PNAS)*, could lead to treatments for autism and other disorders thought to be tied to brain changes that occur when the developing brain is very susceptible to inputs from the outside world. Nature--in the form of genes--and nurture--in the form of environmental influences--are fundamentally intertwined during this period.

"Our work points to how a disorder can be genetic and yet be dependent on the environment," said co-author Mriganka Sur, Sherman Fairchild Professor of Neuroscience at the Picower Institute and chair of MIT's brain and cognitive sciences department. "Many genes require activity to be expressed and make their assigned proteins. They alter their expression when activity is altered. Thus, we reveal an important mechanism of brain development that should open up a window into the mechanisms and treatment of brain disorders such as autism."

In the brain, some genes are only expressed, or turned on, in response to stimulus from the outside world. Like a panel of switches that turn lights on and off, genes that don't receive electricity don't "turn on" and express their particular proteins.

Sur and colleagues found a set of novel genes--including a calcium

sensor called cardiac Troponin C, or cTropC--particularly sensitive to a critical period of development. The lack of proteins from these genes during a key phase of development could be one of the culprits in developing autism.

Researchers have long investigated the molecular mechanisms involved in monocular deprivation--when one eye is deprived of sight during a critical period of brain development, that eye becomes permanently blind, even after it is uncovered. This phenomenon is considered an important model for brain development because synapses for the covered eye--deprived of environmental stimulus, or what Sur calls "nurture"--shrivel up or get reassigned to other uses.

Sur and his colleagues looked at which genes are expressed, and which are not, when this phenomenon occurs. They hoped to pin down the correlation between nature--meaning the genes--and the external environment, or nurture. By identifying which genes are particularly apt to switch their expression patterns in response to "nurture," the researchers potentially narrowed down the ones that may be implicated in developmental disorders.

Researchers believe autism spectrum disorders are tied to brain changes that occur during critical periods of development. Different but overlapping critical periods are thought to exist for various cognitive functions affected in autism, such as language and social behaviors.

"Autism is a strongly genetic disorder: genes set up risk factors but by themselves simply make proteins," Sur said. "Genes work together with other influences. In the case of autism, these influences are unknown but could be molecules made by other genes or chemicals from the environment."

If scientists understood how genes changed in response to environmental

influences during this crucial developmental period, they might be able to one day prevent or reverse the changes.

In addition to Sur, authors are Alvin W. Lyckman, a former MIT postdoctoral associate now at Tufts University; MIT brain and cognitive sciences graduate students Sam H. Horng and Cortina L. McCurry; Picower Institute postdoctoral fellows Daniela Tropea and Audra Van Wart and colleagues from other institutions.

Provided by MIT